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Cytotoxicity and actin-depolymerizing activity of aplyronine A, a potent antitumor macrolide of marine origin, and its analogs

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Abstract—Artificial analogs of aplyronine A (**1**), a potent antitumor macrolide, were synthesized and structure–activity (cytotoxicity and actin-depolymerizing activity) relationships were investigated; the side-chain in **1** was found to play a key role in both biological activities.

We previously isolated[1] aplyronine A (**1**) as a potent cytotoxic and antitumor substance from the sea hare *Aplysia kurodai*, and determined its absolute stereostructure,[2] which was confirmed by its total synthesis.[3] Subsequently, we investigated the structure–cytotoxicity relationships of aplyronine A (**1**) using its natural and artificial analogs,[3d] and found that (1) the trimethylserine moiety, two hydroxyl groups, and the side-chain in **1** are responsible for its strong cytotoxicity, and (2) the *N*-formyl enamine part and the dimethylalanine moiety in **1** do not play an important role in its strong cytotoxicity.[3d]

The target biomolecules of aplyronine A (**1**) were investigated: **1** did not interact with DNA, tubulins, or cell cycle-regulating enzymes, but inhibited the polymerization of globular actin (G-actin) to fibrous actin (F-actin) and depolymerized F-actin to G-actin by severing.[4] Actin is one of the most abundant and common proteins in the cytoskeleton and regulates various cell functions, such as muscle contraction, cell motility, and cell division. To date, a few antitumor substances that interact with actin have been reported. Thus, aplyronine A (**1**) is considered a new type of antitumor substance from the standpoint of its mode of

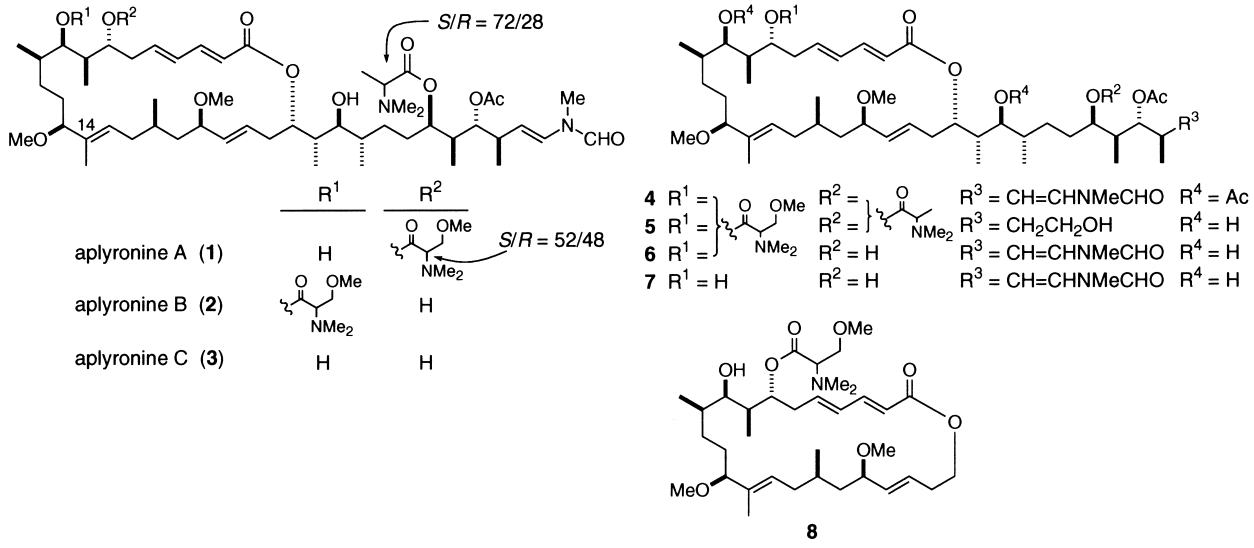

Figure 1. Natural aplyronines and the previously synthesized artificial analogs.

Keywords: marine metabolites; analogs; synthesis; cytotoxicty; actin-depolymerizing; structure–activity.
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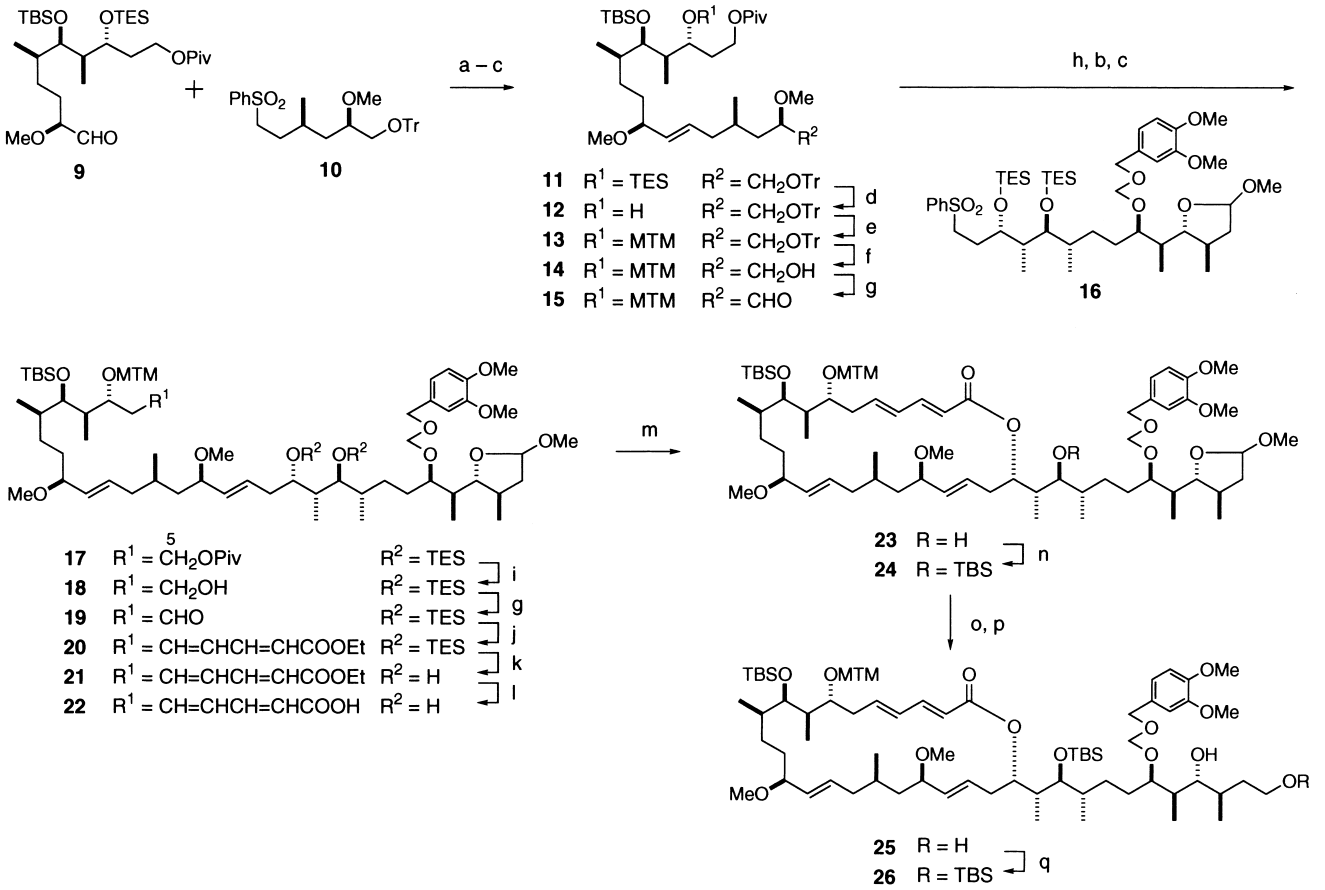


Scheme 1. (a) **10**, BuLi, THF, −78°C, then **9**, −78°C; (b) Ac_2O, DMAP, pyridine, rt; (c) 5% Na–Hg, Na_2HPO_4, MeOH, 0°C; (d) AcOH, H_2O, THF, rt; (e) DMSO, Ac_2O, AcOH, rt→40°C; (f) HCO_2H, Et_2O, rt; (g) Dess–Martin periodinane, pyridine, CH_2Cl_2, rt; (h) **16**, BuLi, THF, −78°C, then $MgBr_2$, **15**, −78°C; (i) DIBAL, CH_2Cl_2, −78°C; (j) LDA, $(EtO)_2P(O)CH_2CH{=}CHCO_2Et$, THF, −45→0°C; (k) HF·pyridine, pyridine, THF, rt; (l) LiOH, H_2O, MeOH, rt; (m) 2,4,6-trichlorobenzoyl chloride, DMAP, Et_3N, CH_2Cl_2, 23°C; then $Ti(O\text{-}i\text{-}Pr)_4$, CH_2Cl_2, rt; (n) TBSCl, imidazole, DMF, 58°C; (o) HCl, H_2O, DME, rt; (p) $NaBH(OMe)_3$, MeOH, 23°C; (q) TBSCl, Et_3N, DMAP, CH_2Cl_2, 23°C.

action. Among natural products, only cytochalasins and phalloidin were previously known to interact with actin.[5] Recently, some marine macrolides, such as latrunculins,[6] scytophycins,[7] goniodomin,[8] mycalolide B,[9] swinholide A,[10] and bistheonellide,[11] have been shown to exhibit actin-depolymerizing activity.

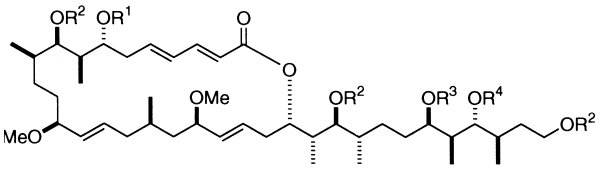
No information is currently available on the structure–actin-depolymerizing activity relationships of **1**, which are interesting with regard to the mode of action of **1**. Recently, we reported the synthesis of artificial analogs of aplyronine A (**1**) and the structure–bioactivity relationships of **1** concerning cytotoxicity and actin-depolymerizing activity.[3d,12] In this article, we describe the synthesis of artificial analogs of **1** and also the updated structure–bioactivity relationships of **1**. Fig. 1 shows natural aplyronines and the previously synthesized analogs of aplyronine A (**1**).[3d]

1. Chemical synthesis

1.1. Synthesis of artificial analogs that lack the C14 methyl group[13]

In the synthesis of aplyronine A (**1**), stereoselective construction of the trisubstituted olefin at C14 was difficult to achieve. Assuming that the C14 methyl group is not important for the biological activities of aplyronine A (**1**), we synthesized four analogs that lack the C14 methyl group, **32**, **36**, **40**, and **43**, which were more readily accessible by organic synthesis than **1**.

These analogs were obtained by a synthetic strategy similar to that for aplyronine A (**1**) from the intermediate **9**[3d] (Scheme 1). Julia olefination[14] between **9** and sulfone **10**[3d] afforded *trans*-olefin **11** (71%). Removal of the TES group in **11** gave alcohol **12** (95%), which was converted to MTM ether **13** (82%). The trityl protecting group in **13** was removed with formic acid to provide alcohol **14** (84%), which was oxidized to aldehyde **15** (82%). Julia olefination of **15** with sulfone **16**[3a] afforded olefin **17** (65%). For four-carbon homologation at C5, removal of the pivaloyl group in **17** and subsequent oxidation led to aldehyde **19** (91%, two steps), which was treated with a Horner–Emmons reagent to afford conjugated diene **20** (88%). Conjugated diene **20** was transformed into a common intermediate **26** (35%) by (1) removal of two TES groups, (2) basic hydrolysis of the ester group to give dihydroxy acid **22**, (3) macrolactonization under Yamaguchi conditions[15] and subsequent isomerization from the 26-membered by-product to **23**, (4) protection of the hydroxy group, (5) acidic hydrolysis of the methyl acetal group followed by reduction



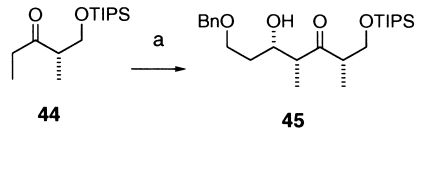
DMBOM = $CH_2OCH_2C_6H_3(OMe)_2$-3,4

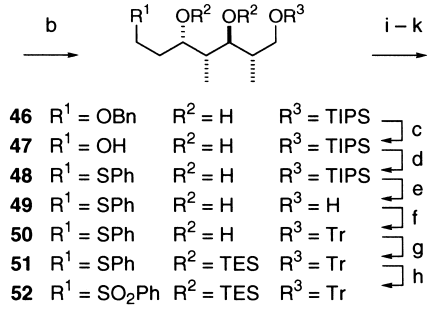
26	R^1 = MTM	R^2 = TBS	R^3 = DMBOM	R^4 = H	a
27	R^1 = MTM	R^2 = TBS	R^3 = DMBOM	R^4 = Ac	b
28	R^1 = MTM	R^2 = TBS	R^3 = H	R^4 = Ac	c
29	R^1 = MTM	R^2 = TBS	R^3 = Me_2Ala	R^4 = Ac	d
30	R^1 = H	R^2 = TBS	R^3 = Me_2Ala	R^4 = Ac	e
31	R^1 = Me_3Ser	R^2 = TBS	R^3 = Me_2Ala	R^4 = Ac	f
32	R^1 = Me_3Ser	R^2 = H	R^3 = Me_2Ala	R^4 = Ac	
27	R^1 = MTM	R^2 = TBS	R^3 = DMBOM	R^4 = Ac	d
33	R^1 = H	R^2 = TBS	R^3 = DMBOM	R^4 = Ac	e
34	R^1 = Me_3Ser	R^2 = TBS	R^3 = DMBOM	R^4 = Ac	f
35	R^1 = Me_3Ser	R^2 = H	R^3 = DMBOM	R^4 = Ac	b
36	R^1 = Me_3Ser	R^2 = H	R^3 = H	R^4 = Ac	
26	R^1 = MTM	R^2 = TBS	R^3 = DMBOM	R^4 = H	g
37	R^1 = MTM	R^2 = TBS	R^3 = DMBOM	R^4 = TES	d
38	R^1 = H	R^2 = TBS	R^3 = DMBOM	R^4 = TES	e
39	R^1 = Me_3Ser	R^2 = TBS	R^3 = DMBOM	R^4 = TES	h
40	R^1 = Me_3Ser	R^2 = H	R^3 = H	R^4 = H	
28	R^1 = MTM	R^2 = TBS	R^3 = H	R^4 = Ac	d
41	R^1 = H	R^2 = TBS	R^3 = H	R^4 = Ac	i
42	R^1 = Me_2Gly	R^2 = TBS	R^3 = Me_2Gly	R^4 = Ac	f
43	R^1 = Me_2Gly	R^2 = H	R^3 = Me_2Gly	R^4 = Ac	

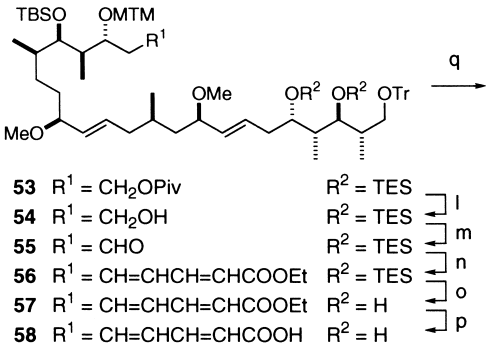
Scheme 2. (a) Ac_2O, DMAP, pyridine, rt; (b) DDQ, CH_2Cl_2, *t*-BuOH, phosphate buffer (pH 6), rt; (c) *N*,*N*-dimethylalanine (*S*/*R*=3:2), DCC, CSA, DMAP, CH_2Cl_2, rt; (d) $AgNO_3$, 2,6-lutidine, H_2O, THF, 30°C; (e) *N*,*N*,*O*-trimethylserine (*S*/*R*=5:2), DCC, CSA, DMAP, CH_2Cl_2, 35°C; (f) HF·pyridine, pyridine, THF, rt; (g) TESCl, imidazole, DMF, 23°C; (h) HCl, H_2O, dioxane, 50°C; (i) *N*,*N*-dimethylglycine, DCC, CSA, DMAP, CH_2Cl_2, rt.

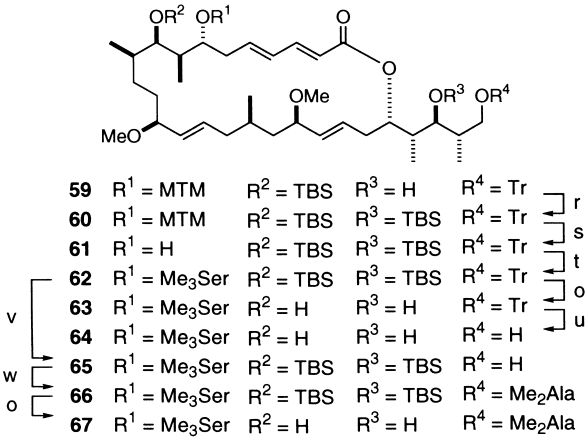
to afford diol **25**, and (6) selective protection of the primary hydroxy group.

From this intermediate **26**, four artificial analogs, **32**, **36**, **40**, and **43**, were synthesized (Scheme 2). Acetylation of **26** and subsequent removal of the [(3,4-dimethoxybenzyl)oxy]-methyl (DMBOM) group[3d,16] afforded alcohol **28** (80%, two steps), which was acylated with *N*,*N*-dimethylalanine (*S*/*R*=3:2) under Keck conditions[17] to afford a 3:1 diastereomeric mixture of dimethylalanine ester **29** quantitatively. The *R*/*S* ratio of the amino acid moiety in **29** was different from that of the *N*,*N*-dimethylalanine used because dynamic kinetic resolution[18] occurred under the acylation conditions. The MTM protecting group in **29** was removed (80%), and the resulting alcohol **30** was acylated with *N*,*N*,*O*-trimethylserine under Keck conditions to give a diastereomeric mixture of trimethylserine ester **31** (72%, *R*/*S*=3:1). Finally, all of the TBS ether groups were removed with HF·pyridine to provide analog **32** (80%). Analogs **36**, **40**, and **43** were also prepared from compound **26** in overall respective yields of 40, 29, and 45%, by using a strategy similar to that in the synthesis of **32**.

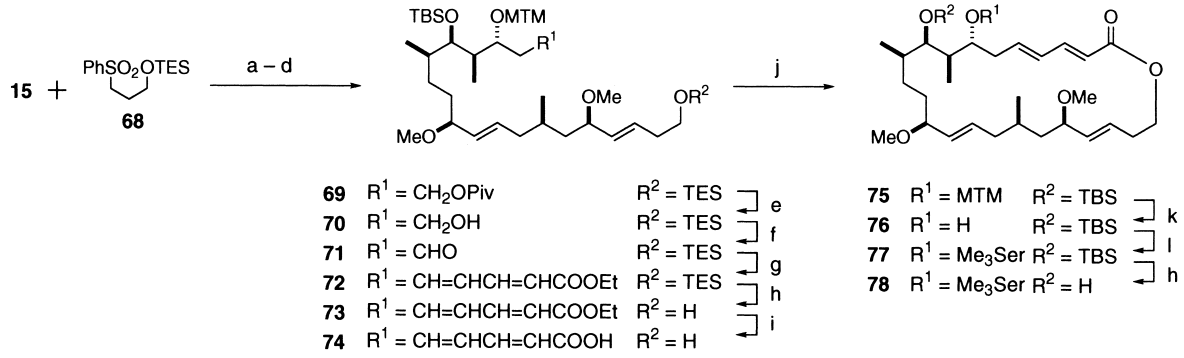








Scheme 3. (a) $Sn(OTf)_2$, Et_3N, CH_2Cl_2, −78°C, then 3-(benzyloxy)propanal, −78°C→−20°C; (b) $Me_4NBH(OAc)_3$, MeCN, AcOH, −20°C; (c) H_2, 20% $Pd(OH)_2$–C, dioxane, rt; (d) $(PhS)_2$, Bu_3P, DMF, 0°C→rt; (e) Bu_4NF, THF, rt; (f) TrCl, pyridine, 50°C; (g) TESCl, imidazole, DMF, 50°C; (h) mCPBA, $NaHCO_3$, CH_2Cl_2, 0°C→rt; (i) **52**, BuLi, THF, −78°C, then $MgBr_2$, **15**, −78°C; (j) Ac_2O, DMAP, pyridine, rt; (k) 5% Na–Hg, Na_2HPO_4, MeOH, 0°C; (l) DIBAL, CH_2Cl_2, −78°C; (m) Dess–Martin periodinane, pyridine, CH_2Cl_2, rt; (n) LDA, $(EtO)_2P(O)CH_2CH$=CH-CO_2Et, THF, −40→0°C; (o) HF·pyridine, pyridine, THF, rt; (p) LiOH, MeOH, H_2O, rt; (q) 2,4,6-trichlorobenzoyl chloride, DMAP, Et_3N, CH_2Cl_2, rt; (r) TBSCl, imidazole, DMF, 60°C; (s) $AgNO_3$, 2,6-lutidine, H_2O, THF, 30°C; (t) *N*,*N*,*O*-trimethylserine (*S*/*R*=5:2), DCC, CSA, DMAP, CH_2Cl_2, 35°C; (u) HCl, H_2O, dioxane, 50°C; (v) HCO_2H, Et_2O, 26°C; (w) *N*,*N*-dimethylalanine (*S*/*R*=3:2), DCC, CSA, DMAP, CH_2Cl_2, rt.



Scheme 4. (a) **68**, BuLi, THF, −78°C, then $MgBr_2$, **15**, −78°C; (b) Ac_2O, DMAP, pyridine, rt; (c) 5% Na–Hg, Na_2HPO_4, MeOH, 0°C; (d) TESCl, imidazole, DMF, 50°C; (e) DIBAL, CH_2Cl_2, −78°C; (f) Dess–Martin periodinane, pyridine, CH_2Cl_2, rt; (g) LDA, $(EtO)_2P(O)CH_2CH{=}CHCO_2Et$, THF, −40→0°C; (h) HF·pyridine, pyridine, THF, rt; (i) LiOH, MeOH, H_2O, rt; (j) PPh_3, DEAD, toluene, −10→4°C; (k) $AgNO_3$, 2,6-lutidine, H_2O, THF, 30°C; (l) *N*,*N*,*O*-trimethylserine (*S*/*R*=5:2), DCC, CSA, DMAP, CH_2Cl_2, 35°C.

1.2. Synthesis of artificial analogs with shorter side-chains and an artificial analog without a side-chain

To investigate the relationship between the length of the side-chain and the biological activities of artificial analogs, three analogs, **64**, **67**, and **78**, were prepared (Schemes 3 and 4).

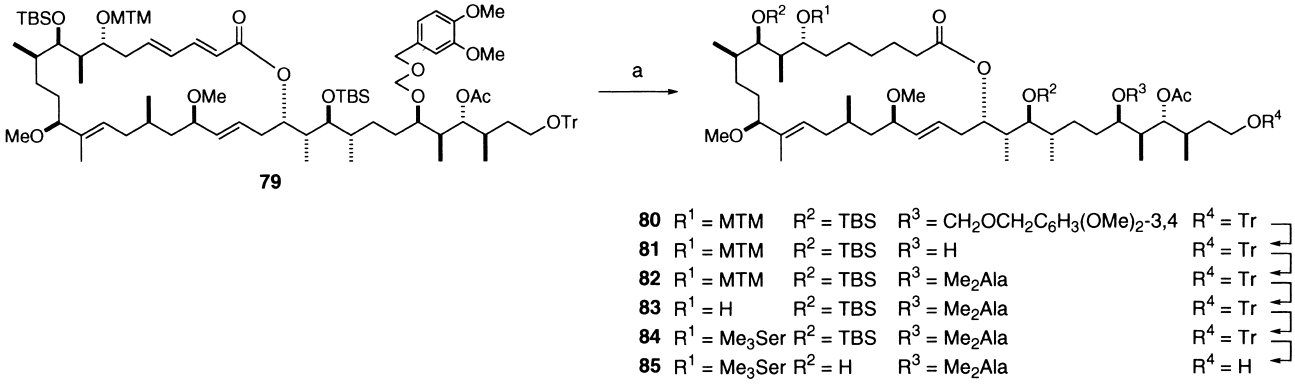
The analogs with a shorter side-chain, **64** and **67**, were prepared from compounds **15** and **52** by a strategy similar to that for aplyronine A (**1**). While compound **52** with four contiguous *syn–anti–anti* stereocenters was previously prepared using the Evans aldol reaction and Sharpless asymmetric epoxidation as key steps,[3a] the improved synthesis of **52** has been achieved by using the Paterson aldol reaction[19] as a key step. Thus, Paterson aldol reaction of ketone **44** and 3-(benzyloxy)propanal gave aldol **45** (83%), stereoselective reduction of which with $Me_4NBH(OAc)_3$[20] afforded diol **46**, which has *syn–anti–anti* stereochemistry (80%).

Hydrogenolysis of the benzyl ether group in **46** followed by substitution of the resulting hydroxy group with the phenylthio group gave sulfide **48** (93%, two steps). After removal of the triisopropylsilyl (TIPS) group in **48**, the primary and secondary hydroxy groups were protected as the trityl and TES ethers, respectively (85%, three steps). Oxidation of sulfide group in **51** provided sulfone **52** (98%). Julia olefination of **52** with aldehyde **15** followed by the same sequence of reactions that were used to convert **17** into **21** gave diol **57** (50%, seven steps). Hydrolysis of the ester group in **57** and subsequent macrolactonization under Yamaguchi conditions afforded lactone **59** (62%, two steps), which was transformed into analog **64** in five steps (52%). Analog **67** was prepared from the intermediate **62** in three steps (52%).

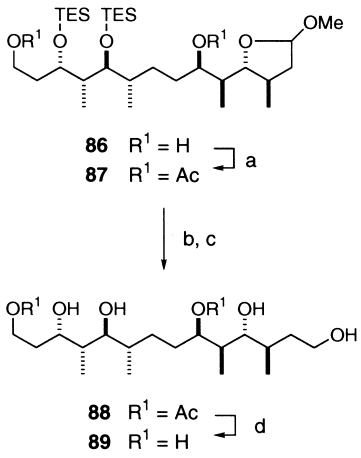
An artificial analog without a side-chain, **78**, was synthesized from **15** in 22% overall yield using the same strategy as for analog **8**,[3d] except for the macrolactonization conditions. Whereas hydroxy acid **74** gave lactone **75** in poor yield under Yamaguchi lactonization conditions, lactone **75** was obtained from **74** in ca. 70% yield under Mitsunobu lactonization conditions.[21]

1.3. Synthesis of a tetrahydro analog

A tetrahydro analog that lacks a conjugated diene group, **85**, was synthesized from the synthetic intermediate **79**[3d] of aplyronine A (**1**) (Scheme 5). Compound **79** was reduced with $NaBH_4$–$NiCl_2$[22] to give lactone **80** (69%), which was converted into analog **85** in 51% overall yield by the same sequence of reactions that was used to convert **27** into **32**.



Scheme 5. (a) $NaBH_4$, $NiCl_2{\cdot}6H_2O$, MeOH, CH_2Cl_2, 0°C; (b) DDQ, CH_2Cl_2, *t*-BuOH, phosphate buffer (pH 6), rt; (c) *N*,*N*-dimethylalanine (*S*/*R*=3:2), DCC, CSA, DMAP, CH_2Cl_2, rt; (d) $AgNO_3$, 2,6-lutidine, H_2O, THF, 30°C; (e) *N*,*N*,*O*-trimethylserine (*S*/*R*=5:2), DCC, CSA, DMAP, CH_2Cl_2, 35°C; (f) HF·pyridine, pyridine, THF, rt.



Scheme 6. (a) Ac_2O, DMAP, pyridine, rt; (b) HCl, H_2O, DME, rt; (c) $NaBH_4$, EtOH, 0°C; (d) NaOMe, MeOH, rt.

1.4. Synthesis of artificial analogs that only consist of a side-chain

An artificial analog that consists of a side-chain having only hydroxy groups, **89**, was prepared from the synthetic intermediate **86**[3d] of aplyronine A (**1**) in four steps in 60% overall yield (Scheme 6).

Another artificial analog that consists of the same side-chain as aplyronine A (**1**) has, **102**, was also prepared from **86** (Scheme 7). Suitable protecting groups were introduced into **86** to afford compound **93** (85%). By a seven-step sequence of reactions, compound **93** led to compound **99**, which was further converted into the desired analog **102** (10% from **93**).

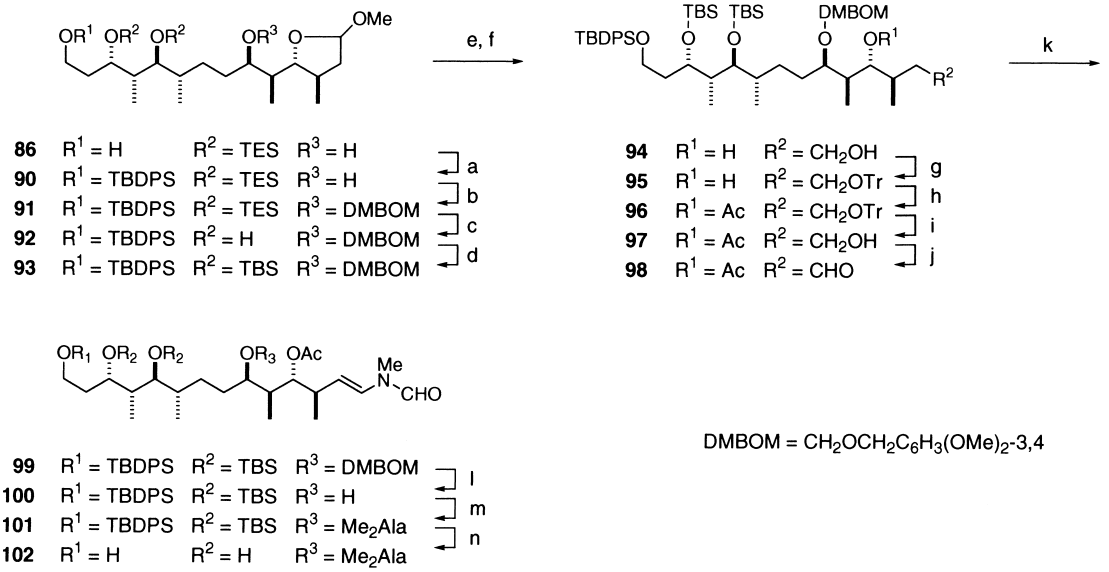
1.5. Synthesis of the acyclic analog

To investigate the importance of the macrocyclic structure of aplyronines for the biological activities, an acyclic analog of **40**, i.e. **111**, was prepared (Scheme 8). Sulfone **104** was prepared from intermediate **16**[3d] in five steps (45%). Julia olefination between **104** and **112**[3d] followed by a six-step sequence of reactions gave analog **111** (11%).

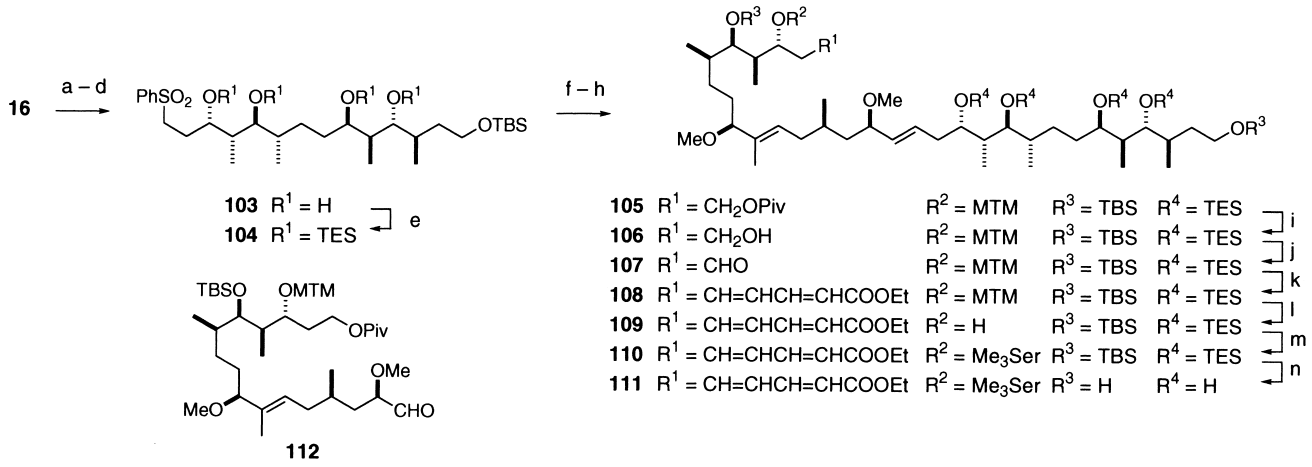
2. Biological activities and discussion

2.1. Structure–cytotoxicity relationships of natural aplyronines and artificial analogs

The cytotoxicity of natural aplyronines and analogs against HeLa S_3 cells is summarized in Table 1. Previously, the side-chain of **1** was found to be essential for its strong cytotoxicity.[3d] In the present study, the effect of the side-chain of **1** on cytotoxicity was evaluated in more detail; comparison of the cytotoxicities of **8**, **36**, and **64** revealed that not only the presence of the side-chain but also its length is crucial for strong cytotoxicity. Comparison of the cytotoxicities of **5** and **85** revealed that the conjugated diene moiety is responsible for the strong cytotoxicity of **1**. Analog **43**, which has two dimethylglycine groups, is about 1000-fold less cytotoxic than analog **32** that has dimethylalanine and trimethylserine groups. This indicates that the structures of the amino acid residues are important for cytotoxicity. One possible explanation for the extremely weak cytotoxicity of **43** is that the dimethylglycine ester groups in **43** might be apt to be hydrolyzed by an esterase in cells to give a compound that is very weakly cytotoxic. The analogs that lack both an *N*-formyl enamine group and a dimethylalanine group, **36** and **40**, are less cytotoxic than those with either of these groups, **5**, **6**, and **32**. This indicates that either of these groups is necessary for the strong cytotoxicity of aplyronine analogs. As expected, the C14 methyl group of **1** was shown to have no significant effect on this activity by comparison of the activities of **5** and **32**.



Scheme 7. (a) TBDPSCl, imidazole, DMF, rt; (b) 3,4-$(MeO)_2C_6H_3CH_2OCH_2Cl$ (DMBOM–Cl),[3d,16] *i*-Pr_2NEt, CH_2Cl_2, rt; (c) AcOH, H_2O, THF, rt; (d) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0°C; (e) HCl, H_2O, DME, rt; (f) $NaBH_4$, EtOH, rt; (g) TrCl, pyridine, 50°C; (h) Ac_2O, DMAP, pyridine, rt; (i) HCO_2H, Et_2O, rt; (j) Dess–Martin periodinane, pyridine, CH_2Cl_2, rt; (k) MeNHCHO, PPTS, hydroquinone, MS 3 Å, benzene, reflux; (l) DDQ, CH_2Cl_2, *t*-BuOH, phosphate buffer (pH 6), rt; (m) *N*,*N*-dimethylalanine (*S*/*R*=3:2), DCC, CSA, DMAP, CH_2Cl_2, rt; (n) HF·pyridine, pyridine, THF, rt.



Scheme 8. (a) 1 M HCl, DME, rt; (b) $NaBH_4$, EtOH, rt; (c) 2 M HCl, dioxane, 50°C; (d) TBSCl, DMAP, Et_3N, CH_2Cl_2, rt; (e) TESCl, imidazole, DMF, rt; (f) **104**, BuLi, THF, −78°C, then $MgBr_2$, **112**, −78°C; (g) Ac_2O, DMAP, pyridine, rt; (h) 5% Na–Hg, Na_2HPO_4, MeOH, 0°C; (i) DIBAL, CH_2Cl_2, −78°C; (j) Dess–Martin periodinane, pyridine, CH_2Cl_2, rt; (k) LDA, $(EtO)_2P(O)CH_2CH{=}CHCO_2Et$, THF, −40→0°C; (l) $AgNO_3$, 2,6-lutidine, H_2O, THF, 30°C; (m) *N*,*N*,*O*-trimethylserine (*S*/*R*=5:2), DCC, CSA, DMAP, CH_2Cl_2, 35°C; (n) HF·pyridine, pyridine, THF, 0°C.

2.2. Structure–actin-depolymerizing activity relationships of natural aplyronines and artificial analogs

The actin-depolymerizing activity of natural aplyronines and analogs was determined by flow birefringence, as shown in Table 1. Fibrous particles, such as F-actin, in a flowing liquid are oriented by the shearing force. Determination of the extent of the orientation of actin by flow birefringence makes it possible to evaluate the extent of polymerization of actin.[23] The natural and artificial analogs with side-chains of the same length as in aplyronine A (**1**) exhibit strong activity comparable to that of **1**, whereas those with a shorter side-chain, **64** and **67**, are approximately 100 times less active than **1**, and that without a side-chain, **78**, is totally inactive. It is interesting that even a simple hexaol that mimics the side-chain of aplyronine A (**1**), **89**, exhibits actin-depolymerizing activity, although this activity is very weak. More interesting is the finding that the analog that only consists of the side-chain part of aplyronine A (**1**), **102**, exhibits relatively strong activity considering the size of the molecule. These results indicate that (1) the side-chain in **1** plays a key role in its activity, (2) the functional groups in the side-chain greatly enhance the activity, and (3) the combination of a side-chain and the macrolide moiety is essential for the potent activity of **1**. In addition, comparison of the activities of **40** and **111** suggests that the macrocyclic structure of **1** is not so important for its actin-depolymerizing activity. The C14 methyl group and the

Table 1. Cytotoxicity and actin-depolymerizing activity of natural aplyronines and artificial analogs

Compound	Cytotoxicity against HeLa S_3 cells		Actin-depolymerizing activity[a]	
	IC_{50} (ng/mL)	Relative potency[b]	IC_{50}[c] (μM)	Relative potency[b]
Aplyronine A (**1**)	0.48[d]	100	31	100
Aplyronine B (**2**)	3.11[d]	15	33	94
Aplyronine C (**3**)	21.2[d]	2.3	32	97
4	216[d]	0.22	57	54
5	1.72[d]	28	78	40
6	1.03[d]	47	35	86
7	113[d]	0.42	35	86
8	2100[d]	0.023	n.d.	
32	2.6	18	38	82
36	37	1.3	36	86
40	83	0.58	190	16
43	>2000	<0.02	49	63
64	>2000	<0.02	4500[e]	0.69
67	n.d.		1800	1.7
78	n.d.		Inactive	
85	57	0.84	70	44
89	n.d.		7600[e]	0.41
102	n.d.		330	9.9
111	n.d.		460	6.7

[a] Activity was monitored by measuring flow birefringence. For the conditions of the biological assay, see Section 3.
[b] The relative potencies were calculated from the IC_{50} values of the compounds (aplyronine A=100).
[c] IC_{50} is the concentration required to depolymerize F-actin (40 μM) to 50% of its control amplitude.
[d] Ref. 3d.
[e] An exact IC_{50} value could not be obtained because of the limited solubility of the test compound.

N-formylenamine part in aplyronine A (**1**) were also not important for the strong activity of **1**, as in the case of the cytotoxicity of **1**, by comparing the activities of **1**, **5**, and **32**. Other functional groups, such as amino acid residues, two hydroxyl groups, and the conjugated diene moiety, had little effect on the actin-depolymerizing activity of **1**, in contrast to their relation to cytotoxicity.

In conclusion, structure–cytotoxicity relationships and structure–actin-depolymerizing activity relationships of aplyronine A (**1**) were determined to a considerable extent. The side-chain of aplyronine A (**1**) proved to play a key role in both of these biological activities of **1**.

3. Experimental

3.1. General

Optical rotations were recorded on a JASCO DIP-1000 polarimeter. UV spectra were obtained on a JASCO V-550 spectrophotometer and IR spectra were measured on a JASCO FT/IR-230 spectrophotometer. ^{1}H NMR spectra were recorded on a JEOL EX-270 (270 MHz), A-400 (400 MHz), or A-600 (600 MHz) spectrometer with TMS as an internal reference. FABMS spectra and high-resolution FABMS analysis were performed in *m*-nitrobenzyl alcohol on a JEOL LG-2000 spectrometer. Column chromatography was carried out on a Fuji Silysia silica gel BW-820MH unless otherwise noted. All solvents and chemicals were purified by standard procedures.

3,4-Dimethoxybenzyloxymethyl chloride (DMBOM–Cl) was prepared from 3,4-dimethoxybenzyl alcohol by the procedure for $CH_3OC_6H_4CH_2OCH_2Cl$.[24]

3.1.1. Julia coupling reaction of aldehyde 9 with sulfone 10. To a stirred solution of sulfone **10**[3d] (167 mg, 0.316 mmol) in THF (2 mL) cooled at −78°C was added a 1.58 M solution of BuLi in hexane (0.20 mL, 0.316 mmol) dropwise. After the mixture was stirred at −78°C for 30 min, a solution of aldehyde **9**[3d] (75.5 mg, 0.132 mmol) in THF (1.0 mL) was added dropwise, and the resulting mixture was stirred at −78°C for 135 min. The reaction was quenched by adding saturated aqueous NH_4Cl (5 mL), and the mixture was extracted with Et_2O (3×10 mL). The combined extracts were washed with brine (5 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (50 g, hexane–Et_2O 5:1→3:1→2:1→1:1) to give a diastereomeric mixture of hydroxy sulfones (127 mg) as a colorless oil along with recovered **10** (83 mg, 50%). The hydroxy sulfones were used in the next experiment without separation of the diastereomers.

To a stirred solution of the diastereomeric mixture of hydroxy sulfones (127 mg) in pyridine (1.2 mL) were added Ac_2O (0.6 mL) and DMAP (6.3 mg, 0.052 mmol) at room temperature. The mixture was stirred at room temperature for 2 h and concentrated. The residue was purified by column chromatography on silica gel (10 g, hexane–Et_2O 2:1→1:1→1:2) to give a diastereomeric mixture of acetoxy sulfones (125 mg) as a colorless oil. The acetoxy sulfones were used in the next experiment without separation of the diastereomers.

To a vigorously stirred solution of the diastereomeric mixture of acetoxy sulfones (164 mg) in MeOH (2 mL) cooled at 0°C were added Na_2HPO_4 (323 mg, 2.28 mmol) and 5% Na–Hg (492 mg, 1.07 mmol). The mixture was stirred at 0°C for 100 min, diluted with saturated aqueous NH_4Cl (5 mL), stirred at room temperature for 1 h, and extracted with Et_2O (3×10 mL). The combined extracts were washed with brine (6 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (14 g, hexane–Et_2O 15:1→10:1→5:1→1:1→1:2) to give a mixture of olefins. Further purification of olefins by medium-pressure liquid chromatography (Fuji Silysia, FL-60D, 6.4 g, hexane–*t*-BuOMe 15:1, 2 mL/min) afforded *E*-olefin **11** (73.4 mg, 71% from **9**) and *Z*-olefin (14 mg, 14% from **9**) as a colorless oil, respectively. **11**: $[\alpha]_D^{27}$=+18.6 (*c* 0.95, $CHCl_3$); IR ($CHCl_3$) 1720, 1600, 1460, 1380, 1285, 1255, 1165, 840 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.48–7.45 (m, 6H), 7.33–7.22 (m, 9H), 5.52 (td, *J*=6.9, 15.2 Hz, 1H), 5.20 (dd, *J*=8.3, 15.2 Hz, 1H), 4.22 (td, *J*=5.5, 11.0 Hz, 1H), 4.04 (td, *J*=7.3, 11.0 Hz, 1H), 3.68 (td, *J*=4.0, 7.3 Hz, 1H), 3.45–3.32 (m, 3H), 3.42 (s, 3H), 3.19 (s, 3H), 3.11 (d, *J*=4.3 Hz, 2H), 2.12 (ddd, *J*=5.5, 7.3, 12.2 Hz, 1H), 1.89–1.72 (m, 2H), 1.72–1.30 (m, 9H), 1.19 (s, 9H), 0.96, (t, *J*=7.9 Hz, 9H), 0.89–0.85 (m, 9H), 0.88 (s, 9H), 0.60 (q, *J*=7.9 Hz, 6H), 0.03 (s, 6H); MS (FAB) *m/z* 947 $(M+Na)^+$; HRMS (FAB) calcd for $C_{57}H_{92}NaO_7Si_2$ $[(M+Na)^+]$ 947.6279, found 947.6279. *Z*-Olefin: $[\alpha]_D^{20}$=+12.1 (*c* 1.34, $CHCl_3$); IR ($CHCl_3$) 1720, 1460, 1450, 1285, 1250, 835 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.49–7.43 (m, 6H), 7.33–7.19 (m, 9H), 5.54 (ddd, *J*=6.3, 8.6, 11.2 Hz, 1H), 5.25 (dd, *J*=9.3, 11.2 Hz, 1H), 4.22 (td, *J*=5.5, 11.0 Hz, 1H), 4.04 (td, *J*=7.3, 11.0 Hz, 1H), 3.84 (m, 1H), 3.68 (td, *J*=4.0, 7.3 Hz, 1H), 3.42 (s, 3H), 3.35 (m, 2H), 3.20 (s, 3H), 3.11 (d, *J*=4.3 Hz, 2H), 2.10–1.86 (m, 3H), 1.89–1.40 (m, 10H), 1.19 (s, 9H), 0.95, (t, *J*=7.9 Hz, 9H), 0.89–0.84 (m, 9H), 0.88 (s, 9H), 0.60 (q, *J*=7.9 Hz, 6H), 0.03 (s, 6H); MS (FAB) *m/z* 967 $(M+Na)^+$; HRMS (FAB) calcd for $C_{57}H_{92}NaO_7Si_2$ $[(M+Na)^+]$ 967.6279, found 967.6290.

3.1.2. Alcohol 12. To a stirred solution of *E*-olefin **11** (267 mg, 0.283 mmol) in THF (4 mL) was added a 4:1 mixture of AcOH and H_2O (5 mL), and the mixture was stirred at room temperature for 6 h. The mixture was poured into saturated aqueous $NaHCO_3$ (25 mL) cooled at 0°C, and the aqueous mixture was extracted with Et_2O (3×80 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (15 mL) and brine (15 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (16 g, hexane–Et_2O 10:1→5:1→3:1→1:1) to give **12** (223 mg, 95%) as a colorless oil: $[\alpha]_D^{26}$=+14.7 (*c* 0.97, $CHCl_3$); IR ($CHCl_3$) 3430 (br), 1720, 1600, 1450, 1285, 1255, 1165, 840 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.48–7.44 (m, 6H), 7.33–7.19 (m, 9H), 5.52 (ddd, *J*=6.9, 6.9, 15.2 Hz, 1H), 5.20 (dd, *J*=8.3, 15.2 Hz, 1H), 4.33 (ddd, *J*=5.0, 8.6, 11.4 Hz, 1H), 4.20 (ddd, *J*=5.3, 5.9, 11.4 Hz, 1H), 3.81 (dd, *J*=1.7, 5.0 Hz, 1H), 3.54 (m, 1H), 3.42 (s, 3H), 3.37 (m, 2H), 3.20 (s, 3H), 3.11 (d, *J*=4.6 Hz, 2H), 3.01 (d, *J*=4.0 Hz, 1H, OH), 2.11 (m, 1H), 1.98–1.75 (m, 2H), 1.68–1.35 (m, 9H), 1.20

(s, 9H), 0.89–0.86 (m, 3H), 0.89 (s, 9H), 0.85 (d, J=6.6 Hz, 6H), 0.83 (d, J=6.6 Hz, 3H), 0.06 (s, 3H), 0.05 (s, 3H); MS (FAB) m/z 853 $(M+Na)^+$.

3.1.3. MTM ether 13. To a stirred solution of alcohol **12** (203 mg, 0.246 mmol) in DMSO (1 mL) was added a 1:5.6 mixture of AcOH and Ac_2O (0.825 mL) at room temperature. The mixture was stirred at room temperature for 2 h and at 40°C for 5 h. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (20 mL) cooled at 0°C, and the aqueous mixture was extracted with Et_2O (3×30 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (30 g, hexane–Et_2O 10:1→7:1→5:1→1:1) to give **13** (182 mg, 82%) as a colorless oil: $[\alpha]_D^{26}$=+42.4 (c 1.07, $CHCl_3$); IR ($CHCl_3$) 1720, 1600, 1450, 1285, 1255, 1160, 835 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.48–7.45 (m, 6H), 7.36–7.23 (m, 9H), 5.52 (td, J=6.9, 15.2 Hz, 1H), 5.21 (dd, J=8.3, 15.2 Hz, 1H), 4.64 (d, J=11.9 Hz, 1H), 4.57 (d, J=11.9 Hz, 1H), 4.45 (m, 2H), 3.63 (m, 1H), 3.50 (t, J=3.6 Hz, 1H), 3.42 (s, 3H), 3.38 (m, 2H), 3.20 (s, 3H), 3.11 (d, J=4.9 Hz, 2H), 2.15 (s, 3H), 2.11 (m, 1H), 1.96 (m, 1H), 1.89–1.68 (m, 2H), 1.65–1.33 (m, 9H), 1.20 (s, 9H), 0.90–0.84 (m, 9H), 0.89 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); MS (FAB) m/z 913 $(M+Na)^+$; HRMS (FAB) calcd for $C_{53}H_{82}NaO_7SSi$ $[(M+Na)^+]$ 913.5448, found 913.5430.

3.1.4. Alcohol 14. To a stirred solution of MTM ether **13** (80.6 mg, 0.0906 mmol) in Et_2O (0.75 mL) was added HCOOH (0.5 mL), and the mixture was stirred at 26°C for 30 min. The mixture was poured into saturated aqueous $NaHCO_3$ (10 mL) cooled at 0°C, and the resulting mixture was extracted with Et_2O (30 mL, 20 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (5 g, hexane–Et_2O 5:1→1:1→1:2) to give **14** (49.0 mg, 84%) as a colorless oil: $[\alpha]_D^{27}$=+31.4 (c 1.00, $CHCl_3$); IR ($CHCl_3$) 3630, 3460 (br), 1720, 1285, 1255, 1165, 840 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 5.56 (ddd, J=6.9, 6.9, 15.2 Hz, 1H), 5.25 (dd, J=8.3, 15.2 Hz, 1H), 4.64 (d, J=11.5 Hz, 1H), 4.57 (d, J=11.5 Hz, 1H), 4.22–4.07 (m, 2H), 3.70 (ddd, J=3.0, 6.9, 11.5 Hz, 1H), 3.62 (ddd, J=2.6, 5.0, 8.3 Hz, 1H), 3.51 (t, J=3.6 Hz, 1H), 3.48–3.31 (m, 3H), 3.40 (s, 3H), 3.23 (s, 3H), 2.17 (s, 3H), 2.11 (m, 1H), 2.00–1.35 (m, 12H), 1.20 (s, 9H), 0.91–0.89 (m, 3H), 0.93 (d, J=6.6 Hz, 3H), 0.90 (s, 9H), 0.87 (d, J=6.6 Hz, 3H), 0.06 (s, 3H), 0.05 (s, 3H); MS (FAB) m/z 671 $(M+Na)^+$; HRMS (FAB) calcd for $C_{34}H_{68}NaO_7SSi$ $[(M+Na)^+]$ 671.4352, found 671.4385.

3.1.5. C5–C20 Segment 15. To a stirred solution of alcohol **14** (89.4 mg, 0.138 mmol) in CH_2Cl_2 (0.9 mL) were added pyridine (0.11 mL, 1.4 mmol) and the Dess–Martin periodinane, $C_6H_4(COO)I(OAc)_3$ (71.0 mg, 0.167 mmol), at room temperature. After the mixture was stirred at room temperature for 15 min, Et_2O (1 mL), saturated aqueous $NaHCO_3$ (1 mL), and saturated aqueous $Na_2S_2O_3$ (1 mL) were added. The aqueous mixture was stirred at room temperature for 40 min and extracted with Et_2O (3×5 mL). The combined extracts were washed with H_2O (2 mL) and brine (2 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (4 g, hexane–Et_2O 5:1→3:1→1:1) to give **15** (72.6 mg, 82%) as a colorless oil: $[\alpha]_D^{30}$=+63.4 (c 1.22, $CHCl_3$); IR ($CHCl_3$) 2710, 1730, 1460, 1285, 1250, 1165, 835 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 9.62 (d, J=2.4 Hz, 1H), 5.54 (td, J=6.9, 15.2 Hz, 1H), 5.25 (dd, J=8.3, 15.2 Hz, 1H), 4.63 (d, J=11.2 Hz, 1H), 4.57 (d, J=11.2 Hz, 1H), 4.14 (m, 2H), 3.61 (m, 1H), 3.50 (t, J=3.9 Hz, 1H), 3.43 (s, 3H), 3.42 (m, 1H), 3.22 (s, 3H), 2.15 (s, 3H), 2.13 (m, 1H), 1.99–1.36 (m, 13H), 1.19 (s, 9H), 0.93 (d, J=6.8 Hz, 3H), 0.88 (d, J=6.8 Hz, 3H), 0.88 (s, 9H), 0.87 (d, J=6.8 Hz, 3H), 0.05 (s, 3H), 0.04 (s, 3H); MS (FAB) m/z 669 $(M+Na)^+$; HRMS (FAB) calcd for $C_{34}H_{66}NaO_7SSi$ $(M+Na)^+$ 669.4196, found 669.4196.

3.1.6. Olefin 17. To a stirred solution of sulfone **16**[3d] (117 mg, 0.198 mmol) in THF (1 mL) cooled at −78°C was added a 1.57 M solution of BuLi in hexane (0.125 mL, 0.196 mmol) dropwise. After the mixture was stirred at −78°C for 30 min, a 0.25 M solution of $MgBr_2$ in THF (0.89 mL, 0.223 mmol) was added and the mixture was stirred at −78°C for 10 min. A solution of aldehyde **15** (74 mg, 0.115 mmol) in THF (1.0 mL) was added dropwise, and the resulting mixture was stirred at −78°C for 90 min. The reaction was quenched by adding saturated aqueous NH_4Cl (3 mL), and the mixture was extracted with Et_2O (3×10 mL). The combined extracts were washed with brine (4 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (35 g, benzene–EtOAc 20:1→15:1→10:1→5:1) to give a diastereomeric mixture of hydroxy sulfones (160 mg) as a colorless oil along with recovered **16** (81 mg, 45%). The hydroxy sulfones were used in the next experiment without separation of the diastereomers.

To a stirred solution of the diastereomeric mixture of hydroxy sulfones (160 mg) in pyridine (1 mL) were added Ac_2O (0.5 mL) and DMAP (13.3 mg, 0.108 mmol) at room temperature. The mixture was stirred at room temperature for 3.5 h and concentrated. The residue was purified by column chromatography on silica gel (20 g, hexane–Et_2O 2:1→1:1→1:2) to give a diastereomeric mixture of acetoxy sulfones (164 mg) as a colorless oil. The acetoxy sulfones were used in the next experiment without separation of the diastereomers.

To a vigorously stirred solution of the diastereomeric mixture of acetoxy sulfones (164 mg) in MeOH (3 mL) cooled at 0°C were added Na_2HPO_4 (442 mg, 3.11 mmol) and 5% Na–Hg (725 mg, 1.56 mmol). The mixture was stirred at 0°C for 35 min, diluted with saturated aqueous NH_4Cl (3 mL), stirred at room temperature for 1 h, and extracted with Et_2O (3×20 mL). The combined extracts were washed with brine (5 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (20 g, hexane–Et_2O 5:1→3:1→2:1→1:1) to give a mixture of olefins. Further purification of olefins by medium-pressure liquid chromatography (Fuji Silysia, FL-60D, 43 g, benzene–EtOAc (10:1→5:1), 6 mL/min) afforded E-olefin **17** (105 mg, 66% from **15**) and Z-olefin (11 mg, 7% from **15**) as a

colorless oil, respectively. **17**: $[\alpha]_D^{28}$=+31.8 (*c* 0.904, $CHCl_3$); IR ($CHCl_3$) 1720, 1595, 1515, 1460, 1380, 1260, 1160, 1095, 1030, 970, 830 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.92–6.90 (m, 2H), 6.82 (d, *J*=8.3 Hz, 1H), 5.59–5.47 (m, 2H), 5.23 (dd, *J*=8.3, 14.2 Hz, 1H), 5.23 (dd, *J*=8.3, 14.2 Hz, 1H), 4.88 (d, *J*=4.4 Hz, 1H), 4.83 (d, *J*=6.8 Hz, 1H), 4.81 (d, *J*=6.8 Hz, 1H), 4.64 (d, *J*=11.2 Hz, 1H), 4.60 (d, *J*=11.2 Hz, 1H), 4.58 (d, *J*=11.2 Hz, 1H), 4.56 (d, *J*= 11.7 Hz, 1H), 4.20–4.09 (m, 2H), 4.03 (dd, *J*=6.8, 6.8 Hz, 1H), 3.96 (m, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.63–3.30 (m, 6H), 3.27 (s, 3H), 3.23 (s, 3H), 3.21 (s, 3H), 2.33–1.36 (m, 25H), 2.16 (s, 3H), 1.20 (s, 9H), 1.09 (d, *J*=6.8 Hz, 3H), 0.97–0.86 (m, 9H), 0.95 (t, *J*=7.8 Hz, 9H), 0.95 (t, *J*= 7.8 Hz, 9H), 0.90 (s, 9H), 0.88 (d, *J*=6.8 Hz, 3H), 0.87 (d, *J*=6.8 Hz, 3H), 0.78 (d, *J*=6.8 Hz, 3H), 0.60 (q, *J*=7.8 Hz, 6H), 0.59 (q, *J*=7.8 Hz, 6H), 0.06 (s, 3H), 0.05 (s, 3H); MS (FAB) *m/z* 1405 $(M+Na)^+$; HRMS (FAB) calcd for $C_{75}H_{142}NaO_{14}SSi_3$ $[(M+Na)^+]$ 1405.9325, found 1405.9270. *Z*-Olefin: $[\alpha]_D^{30}$=+33.0 (*c* 0.656, $CHCl_3$); IR ($CHCl_3$) 1720, 1595, 1515, 1465, 1380, 1260, 1160, 1095, 1030, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.92–6.90 (m, 2H), 6.82 (d, *J*=8.3 Hz, 1H), 5.59–5.47 (m, 2H), 5.23 (dd, *J*=8.3, 14.2 Hz, 1H), 5.23 (dd, *J*=8.3, 14.2 Hz, 1H), 4.88 (d, *J*=4.4 Hz, 1H), 4.83 (d, *J*=6.8 Hz, 1H), 4.81 (d, *J*=6.8 Hz, 1H), 4.64 (d, *J*=11.2 Hz, 1H), 4.60 (d, *J*= 11.2 Hz, 1H), 4.58 (d, *J*=11.2 Hz, 1H), 4.56 (d, *J*=11.7 Hz, 1H), 4.20–4.09 (m, 2H), 4.03 (dd, *J*=6.8, 6.8 Hz, 1H), 3.96 (m, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.63–3.30 (m, 6H), 3.27 (s, 3H), 3.23 (s, 3H), 3.21 (s, 3H), 2.33–1.36 (m, 25H), 2.16 (s, 3H), 1.20 (s, 9H), 1.09 (d, *J*=6.8 Hz, 3H), 0.97–0.86 (m, 9H), 0.95 (t, *J*=7.8 Hz, 9H), 0.95 (t, *J*=7.8 Hz, 9H), 0.90 (s, 9H), 0.88 (d, *J*=6.8 Hz, 3H), 0.87 (d, *J*=6.8 Hz, 3H), 0.78 (d, *J*=6.8 Hz, 3H), 0.60 (q, *J*=7.8 Hz, 6H), 0.59 (q, *J*= 7.8 Hz, 6H), 0.06 (s, 3H), 0.05 (s, 3H); MS (FAB) *m/z* 1405 $(M+Na)^+$; HRMS (FAB) calcd for $C_{75}H_{142}NaO_{14}SSi_3$ $[(M+Na)^+]$ 1405.9325, found 1405.9250.

3.1.7. Alcohol 18. To a stirred solution of *E*-olefin **17** (106 mg, 0.0767 mmol) in CH_2Cl_2 (3 mL) cooled at −78°C was added a 1.0 M solution of DIBAL in hexane (0.31 mL, 0.31 mmol) dropwise. The mixture was stirred at −78°C for 1 h and the reaction was quenched by adding MeOH (0.5 mL) and saturated aqueous potassium sodium tartrate (4 mL). The resulting mixture was warmed to room temperature, stirred for 30 min, and extracted with Et_2O (3×10 mL). The combined extracts were washed with brine (3 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (5 g, hexane–EtOAc 4:1→2:1→1:1) to give **18** (99 mg, 99%) as a colorless oil: $[\alpha]_D^{32}$=+36.8 (*c* 1.03, $CHCl_3$); IR ($CHCl_3$) 3480 (br), 1595, 1515, 1465, 1380, 1260, 1095, 1030, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.92–6.89 (m, 2H), 6.82 (d, *J*=7.9 Hz, 1H), 5.61–5.45 (m, 2H), 5.24 (dd, *J*=8.6, 15.1 Hz, 1H), 5.23 (dd, *J*=8.6, 15.1 Hz, 1H), 4.88 (d, *J*=5.0 Hz, 1H), 4.83 (d, *J*=7.3 Hz, 1H), 4.80 (d, *J*=7.3 Hz, 1H), 4.70 (d, *J*=11.6 Hz, 1H), 4.61 (d, *J*=11.6 Hz, 1H), 4.59 (d, *J*=11.6 Hz, 1H), 4.56 (d, *J*=11.6 Hz, 1H), 4.05–3.93 (m, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.84–3.67 (m, 3H), 3.60–3.41 (m, 5H), 3.27 (s, 3H), 3.24 (s, 3H), 3.21 (s, 3H), 2.43 (t, *J*=5.9 Hz, 1H, –OH), 2.31–1.82 (m, 7H), 2.21 (s, 3H), 1.70–1.37 (m, 17H), 1.10–1.03 (m, 1H), 1.09 (d, *J*=6.6 Hz, 3H), 0.98–0.86 (m, 12H), 0.95 (t, *J*=7.8 Hz, 9H), 0.95 (t, *J*=7.8 Hz, 9H), 0.90 (s, 9H), 0.87 (d, *J*=6.6 Hz, 3H), 0.78 (d, *J*=6.9 Hz, 3H), 0.60 (q, *J*=7.8 Hz, 6H), 0.60 (q, *J*=7.8 Hz, 6H), 0.05 (s, 3H), 0.05 (s, 3H); MS (FAB) *m/z* 1321 $(M+Na)^+$; HRMS (FAB) calcd for $C_{70}H_{134}NaO_{13}SSi_3$ $[(M+Na)^+]$ 1321.8750, found 1321.8750.

3.1.8. Aldehyde 19. The experimental procedure was similar to that described for compound **15**. **19** (91% yield): a colorless oil; $[\alpha]_D^{30}$=+23.6 (*c* 1.11, $CHCl_3$); IR ($CHCl_3$) 2730, 1725, 1595, 1515, 1465, 1380, 1260, 1095, 1030, 970, 835 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 9.82 (t, *J*=2.3 Hz, 1H), 6.92–6.89 (m, 2H), 6.82 (d, *J*=7.9 Hz, 1H), 5.61–5.45 (m, 2H), 5.24 (dd, *J*=8.2, 15.5 Hz, 1H), 5.22 (dd, *J*=8.2, 15.5 Hz, 1H), 4.88 (d, *J*=4.6 Hz, 1H), 4.83 (d, *J*= 7.3 Hz, 1H), 4.80 (d, *J*=7.3 Hz, 1H), 4.67 (d, *J*=11.5 Hz, 1H), 4.61 (d, *J*=11.5 Hz, 1H), 4.60 (d, *J*=11.5 Hz, 1H), 4.55 (d, *J*=11.5 Hz, 1H), 4.08–3.93 (m, 3H), 3.88 (s, 3H), 3.87 (s, 3H), 3.60–3.40 (m, 5H), 3.27 (s, 3H), 3.24 (s, 3H), 3.21 (s, 3H), 2.59–2.55 (m, 2H), 2.31–1.97 (m, 6H), 2.14 (s, 3H), 1.87 (m, 1H), 1.67–1.34 (m, 15H), 1.10–1.01 (m, 1H), 1.09 (d, *J*=6.6 Hz, 3H), 0.98–0.86 (m, 12H), 0.95 (t, *J*=7.9 Hz, 9H), 0.95 (t, *J*=7.9 Hz, 9H), 0.90 (s, 9H), 0.87 (d, *J*=6.6 Hz, 3H), 0.78 (d, *J*=6.9 Hz, 3H), 0.60 (q, *J*=7.9 Hz, 6H), 0.59 (q, *J*=7.9 Hz, 6H), 0.05 (s, 6H); MS (FAB) *m/z* 1319 $(M+Na)^+$; HRMS (FAB) calcd for $C_{70}H_{132}NaO_{13}SSi_3$ $[(M+Na)^+]$ 1319.8595, found 1319.8590.

3.1.9. α,β,γ,δ-Unsaturated ester 20. To a stirred solution of triethyl 4-phosphonocrotonate (50.8 mg, 0.203 mmol) in THF (0.5 mL) cooled at −48°C was added a 0.5 M solution of LDA (0.35 mL, 0.18 mmol). The mixture was stirred at −48°C for 30 min, and a solution of aldehyde **19** (46.0 mg, 0.0355 mmol) in THF (0.8 mL) was added dropwise. The resulting mixture was stirred at −48°C for 10 min and at 0°C for 15 min. The mixture was diluted with saturated aqueous NH_4Cl (2 mL) and extracted with Et_2O (3× 6 mL). The combined extracts were washed with brine (2 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (5 g, hexane–Et_2O 3:1→1:1) to give **20** (4*E*/4*Z*=16:1) (43.6 mg, 88%) as a colorless oil: $[\alpha]_D^{31}$=+6.98 (*c* 1.15, $CHCl_3$); IR ($CHCl_3$) 1705, 1645, 1615, 1595, 1515, 1465, 1365, 1260, 1095, 1025, 970, 835 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) (4*E*-isomer) δ 7.26 (dd, *J*=10.2, 15.1 Hz, 1H), 6.92–6.89 (m, 2H), 6.82 (d, *J*=8.3 Hz, 1H), 6.28–6.13 (m, 2H), 5.80 (d, *J*=15.1 Hz, 1H), 5.59–5.46 (m, 2H), 5.23 (dd, *J*=8.3, 15.1 Hz, 1H), 5.22 (dd, *J*=8.3, 15.1 Hz, 1H), 4.88 (d, *J*= 4.4 Hz, 1H), 4.83 (d, *J*=6.8 Hz, 1H), 4.80 (d, *J*=6.8 Hz, 1H), 4.62 (d, *J*=11.7 Hz, 1H), 4.60 (d, *J*=11.7 Hz, 1H), 4.59 (d, *J*=11.7 Hz, 1H), 4.56 (d, *J*=11.7 Hz, 1H), 4.20 (q, *J*=6.8 Hz, 2H), 4.03 (br dd, *J*=7.3, 7.3 Hz, 1H), 3.96 (m, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.63 (dd, *J*=3.4, 3.4 Hz, 1H), 3.59–3.47 (m, 4H), 3.41 (m, 1H), 3.27 (s, 3H), 3.24 (s, 3H), 3.21 (s, 3H), 2.47 (m, 1H), 2.34–2.12 (m, 5H), 2.15 (s, 3H), 2.09 (dd, *J*=7.3, 12.2 Hz, 1H), 1.90–1.83 (m, 2H), 1.68–1.37 (m, 15H), 1.29 (t, *J*=6.8 Hz, 3H), 1.09 (d, *J*= 6.8 Hz, 3H), 1.06 (m, 1H), 0.95 (t, *J*=7.8 Hz, 9H), 0.95 (t, *J*=7.8 Hz, 9H), 0.94–0.77 (m, 6H), 0.93 (d, *J*=6.8 Hz, 3H), 0.90 (s, 9H), 0.87 (d, *J*=6.8 Hz, 3H), 0.84 (d, *J*=6.8 Hz, 3H), 0.78 (d, *J*=6.8 Hz, 3H), 0.60 (q, *J*=7.8 Hz, 6H), 0.59 (q, *J*=7.8 Hz, 6H), 0.06 (s, 3H), 0.05 (s, 3H); MS (FAB) *m/z* 1415 $(M+Na)^+$; HRMS (FAB) calcd for $C_{76}H_{140}NaO_{14}SSi_3$ $[(M+Na)^+]$ 1415.9170, found 1415.9170.

3.1.10. Diol 21. A solution of α,β,γ,δ-unsaturated ester **20** (4*E*/4*Z*=16:1) (42.0 mg, 0.0302 mmol) in a 5:3:1 mixture of THF, pyridine, and HF·pyridine (1 mL) was stirred at room temperature for 1 h. The mixture was diluted with EtOAc (5 mL) and cooled to 0°C, and then saturated aqueous $NaHCO_3$ (8 mL) was added. The organic layer was separated, and the aqueous layer was extracted with EtOAc (3×10 mL). The organic layer and the extracts were combined, washed with brine (4 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (2 g, hexane–EtOAc 1:1→2:3→1:2) to give **21** (4*E*/4*Z*=16:1) (34.6 mg, 99%) as a colorless oil: $[\alpha]_D^{29}$=+1.17 (*c* 1.19, $CHCl_3$); IR ($CHCl_3$) 3490 (br), 1700, 1640, 1615, 1595, 1515, 1465, 1365, 1260, 1095, 1025, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (4*E*-isomer) δ 7.26 (dd, *J*=10.3, 15.6 Hz, 1H), 6.94–6.90 (m, 2H), 6.83 (d, *J*=8.3 Hz, 1H), 6.28–6.13 (m, 2H), 5.80 (d, *J*=15.6 Hz, 1H), 5.62 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.54 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.34 (dd, *J*=8.3, 15.1 Hz, 1H), 5.23 (dd, *J*=8.3, 15.1 Hz, 1H), 4.90 (d, *J*=4.9 Hz, 1H), 4.86 (d, *J*=6.8 Hz, 1H), 4.83 (d, *J*=6.8 Hz, 1H), 4.63–4.56 (m, 4H), 4.20 (q, *J*=7.3 Hz, 2H), 4.06 (dd, *J*=6.3, 6.3 Hz, 1H), 3.97 (m, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.63 (dd, *J*=3.4, 3.4 Hz, 1H), 3.60–3.54 (m, 3H), 3.42 (m, 1H), 3.30 (m, 1H), 3.30 (s, 3H), 3.23 (s, 3H), 3.23 (s, 3H), 2.77 (d, *J*=2.9 Hz, 1H, –OH), 2.72 (d, *J*=5.4 Hz, 1H, –OH), 2.44 (m, 1H), 2.34–2.05 (m, 6H), 2.15 (s, 3H), 1.92–1.79 (m, 3H), 1.67–1.38 (m, 14H), 1.29 (t, *J*=7.3 Hz, 3H), 1.19–0.87 (m, 13H), 1.10 (d, *J*=6.3 Hz, 3H), 0.97 (d, *J*=7.3 Hz, 3H), 0.89 (s, 9H), 0.84 (d, *J*=6.8 Hz, 3H), 0.06 (s, 3H), 0.05 (s, 3H); MS (FAB) *m/z* 1187 $(M+Na)^+$; HRMS (FAB) calcd for $C_{64}H_{112}NaO_{14}SSi$ $[(M+Na)^+]$ 1187.7439, found 1187.7490.

3.1.11. *seco*-Acid 22. To a stirred solution of diol **21** (4*E*/4*Z*=16:1) (43.1 mg, 0.0370 mmol) in MeOH (4 mL) was added 5 M aqueous LiOH (0.5 mL) at room temperature, and the mixture was stirred at room temperature for 13.5 h. The mixture was diluted with EtOAc (10 mL), cooled to 0°C, and acidified (pH 1) with 1 M aqueous HCl (3 mL). Sodium chloride (2 g) was added to the mixture and the organic layer was separated. The aqueous layer was extracted with EtOAc (3×10 mL). The organic layer and the extracts were combined, washed with brine (4 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (4 g, hexane–EtOAc 1:1→EtOAc) to give **22** (4*E*/4*Z*=16:1) (41.8 mg, 99%) as a colorless oil: $[\alpha]_D^{27}$=−7.7 (*c* 1.06, $CHCl_3$); IR ($CHCl_3$) 3600–2400 (br), 1690, 1640, 1615, 1595, 1515, 1465, 1380, 1260, 1095, 1025, 970, 835 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) (4*E*-isomer) δ 7.29 (dd, *J*=10.7, 15.1 Hz, 1H), 6.94–6.90 (m, 2H), 6.83 (d, *J*=7.8 Hz, 1H), 6.30–6.18 (m, 2H), 5.79 (d, *J*=15.1 Hz, 1H), 5.60 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.53 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.34 (dd, *J*=8.3, 15.1 Hz, 1H), 5.22 (dd, *J*=8.3, 15.1 Hz, 1H), 4.91 (d, *J*=4.9 Hz, 1H), 4.86 (d, *J*=6.8 Hz, 1H), 4.83 (d, *J*=6.8 Hz, 1H), 4.64–4.61 (m, 2H), 4.59 (d, *J*=11.7 Hz, 1H), 4.58 (d, *J*=11.7 Hz, 1H), 4.06 (m, 1H), 3.99 (m, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.63 (dd, *J*=2.9, 3.4 Hz, 1H), 3.60–3.53 (m, 3H), 3.42 (m, 1H), 3.35 (dd, *J*=5.9, 5.9 Hz, 1H), 3.30 (s, 3H), 3.24 (s, 3H), 3.23 (s, 3H), 2.47 (ddd, *J*=4.4, 4.4, 15.6 Hz, 1H), 2.36–2.05 (m, 7H), 2.16 (s, 3H), 1.94–1.78 (m, 3H), 1.67–1.00 (m, 15H), 1.10 (d, *J*=6.8 Hz, 3H), 0.96 (d, *J*=6.8 Hz, 3H), 0.91 (m, 9H), 0.89 (s, 9H), 0.87 (d, *J*=6.8 Hz, 3H), 0.84 (d, *J*=6.8 Hz, 3H), 0.06 (s, 3H), 0.05 (s, 3H). Signals of three protons (COOH, 2×OH) were not observed; MS (FAB) *m/z* 1181 $(M-H+2Na)^+$; HRMS (FAB) calcd for $C_{62}H_{107}Na_2O_{14}SSi$ $[(M-H+2Na)^+]$ 1181.6947, found 1181.6930.

3.1.12. Macrolactonization of *seco*-acid 22. To a stirred solution of *seco*-acid **22** (4*E*/4*Z*=16:1) (29.0 mg, 0.0255 mmol) in CH_2Cl_2 (30 mL) were successively added Et_3N (0.035 mL, 0.25 mmol), DMAP (63.6 mg, 0.52 mmol), and 2,4,6-trichlorobenzoyl chloride (0.035 mL, 0.22 mmol) at room temperature. The mixture was stirred at room temperature for 2.5 h and successively washed with 1 M aqueous HCl (5 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (2 g, hexane–EtOAc 2:1→1:1) and preparative HPLC (Develosil 30-10, 20×250 mm, hexane–EtOAc–MeOH 80:20:1, 6 mL/min) to give the 24-membered lactone **23** (t_R=38 min, 10 mg, 35%) and the 26-membered lactone (t_R=46 min, 8.8 mg, 31%) as a colorless oil, respectively. **23**: $[\alpha]_D^{27}$=+42.9 (*c* 0.968, $CHCl_3$); IR ($CHCl_3$) 3500 (br), 1690, 1640, 1615, 1595, 1515, 1465, 1380, 1260, 1095, 1030, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (m, 1H), 6.93–6.91 (m, 2H), 6.83 (d, *J*=8.3 Hz, 1H), 6.30–6.17 (m, 2H), 5.82 (d, *J*=15.6 Hz, 1H), 5.53 (ddd, *J*=4.4, 10.3, 14.6 Hz, 1H), 5.37 (br d, *J*=10.7 Hz, 1H), 5.28 (ddd, *J*=5.9, 8.3, 14.6 Hz, 1H), 5.17–5.08 (m, 2H), 4.89 (d, *J*=4.9 Hz, 1H), 4.86 (d, *J*=6.8 Hz, 1H), 4.83 (d, *J*=6.8 Hz, 1H), 4.61 (d, *J*=11.7 Hz, 1H), 4.61 (d, *J*=11.7 Hz, 1H), 4.56 (d, *J*=11.7 Hz, 1H), 4.55 (d, *J*=11.7 Hz, 1H), 4.06 (br dd, *J*=6.3, 6.3 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.58–3.39 (m, 3H), 3.56 (dd, *J*=6.8, 10.3 Hz, 1H), 3.41 (ddd, *J*=3.9, 3.9, 9.8 Hz, 1H), 3.27 (s, 3H), 3.25 (s, 3H), 3.20 (s, 3H), 3.17 (d, *J*=4.9 Hz, 1H), 2.99 (m, 1H), 2.50–2.32 (m, 2H), 2.26–2.05 (m, 6H), 2.17 (s, 3H), 1.86 (m, 2H), 1.72–1.09 (m, 15H), 1.10 (d, *J*=6.3 Hz, 3H), 1.01 (d, *J*=6.8 Hz, 3H), 0.93 (d, *J*=6.8 Hz, 3H), 0.89 (s, 9H), 0.89–0.86 (m, 6H), 0.83 (d, *J*=6.8 Hz, 3H), 0.73 (d, *J*=5.9 Hz, 3H), 0.05 (s, 3H), 0.04 (s, 3H); MS (FAB) *m/z* 1141 $(M+Na)^+$; HRMS (FAB) calcd for $C_{62}H_{106}NaO_{13}SSi$ $[(M+Na)^+]$ 1141.7021, found 1141.7010. 26-membered lactone: $[\alpha]_D^{27}$=+20.3 (*c* 1.23, $CHCl_3$); IR ($CHCl_3$) 3500 (br), 1690, 1640, 1615, 1595, 1515, 1465, 1380, 1260, 1095, 1030, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (m, 1H), 6.93–6.91 (m, 2H), 6.83 (d, *J*=8.3 Hz, 1H), 6.30–6.17 (m, 2H), 5.82 (d, *J*=15.6 Hz, 1H), 5.53 (ddd, *J*=4.4, 10.3, 14.6 Hz, 1H), 5.37 (d, *J*=10.7 Hz, 1H), 5.17–5.08 (m, 2H), 4.89 (d, *J*=4.9 Hz, 1H), 4.86 (d, *J*=6.8 Hz, 1H), 4.83 (d, *J*=6.8 Hz, 1H), 4.61 (d, *J*=11.7 Hz, 1H), 4.61 (d, *J*=11.7 Hz, 1H), 4.56 (d, *J*=11.7 Hz, 1H), 4.55 (d, *J*=11.7 Hz, 1H), 4.06 (br dd, *J*=6.3, 6.3 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.58–3.39 (m, 4H), 3.56 (dd, *J*=6.8, 10.3 Hz, 1H), 3.41 (ddd, *J*=3.9, 3.9, 9.8 Hz, 1H), 3.27 (s, 3H), 3.25 (s, 3H), 3.20 (s, 3H), 3.17 (d, *J*=4.9 Hz, 1H), 2.99 (m, 1H), 2.50–2.32 (m, 2H), 2.26–2.05 (m, 6H), 2.17 (s, 3H), 1.86 (m, 2H), 1.72–1.09 (m, 15H), 1.10 (d, *J*=6.3 Hz, 3H), 1.01 (d, *J*=6.8 Hz, 3H), 0.93 (d, *J*=6.8 Hz, 3H), 0.89 (s, 9H), 0.89–0.86 (m, 6H), 0.83 (d, *J*=6.8 Hz, 3H), 0.73 (d, *J*=5.9 Hz, 3H), 0.05 (s, 3H), 0.04 (s, 3H); MS (FAB) *m/z* 1141 $(M+Na)^+$; HRMS (FAB) calcd for $C_{62}H_{106}NaO_{13}SSi$ $[(M+Na)^+]$ 1141.7021, found 1141.6990.

3.1.13. Isomerization of the 26-membered lactone to the 24-membered lactone 23. To a stirred solution of the 26-membered lactone (42.0 mg, 0.0377 mmol) in CH_2Cl_2 (1.8 mL) was added Ti(O-*i*-Pr)$_4$ (0.045 mL, 0.15 mmol) at room temperature. The solution was stirred at room temperature for 13 h and diluted with Et_2O (5 mL) and 0.5 M aqueous (+)-tartaric acid (5 mL). The mixture was stirred at room temperature for 30 min and extracted with Et_2O (3×5 mL). The combined extracts were washed with brine (3 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified as described above to give **84** (28 mg, 66%) along with the recovered 26-membered lactone (7.7 mg, 18%).

3.1.14. Disilyl ether 24. To a stirred solution of the 24-membered lactone **23** (18.2 mg, 0.0163 mmol) and imidazole (131 mg, 1.92 mmol) in DMF (0.16 mL) was added *t*-BuMe$_2$SiCl (119 mg, 0.766 mmol) at room temperature, and the resulting solution was stirred at 60°C for 16 h. The mixture was cooled to room temperature, and ice water (2 g) was added. The mixture was stirred at room temperature for 20 min and extracted with Et_2O (3× 10 mL). The combined extracts were successively washed with 1 M aqueous HCl (3 mL), saturated aqueous $NaHCO_3$ (4 mL), and brine (3 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (2 g, hexane–EtOAc 5:1→4:1→3:1→2:1→1:1) to give **24** (17.0 mg, 85%) as a colorless oil: $[\alpha]_D^{24}$=+36.5 (*c* 1.11, $CHCl_3$); IR ($CHCl_3$) 1705, 1645, 1615, 1595, 1515, 1465, 1375, 1260, 1095, 1030, 970, 835 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (ddd, *J*=4.9, 10.3, 15.1 Hz, 1H), 6.93–6.90 (m, 2H), 6.83 (d, *J*=6.8 Hz, 1H), 6.24–6.16 (m, 2H), 5.80 (d, *J*=15.1 Hz, 1H), 5.54 (ddd, *J*=3.9, 10.3, 14.6 Hz, 1H), 5.30–5.25 (m, 2H), 5.13–5.04 (m, 2H), 4.89 (d, *J*=4.4 Hz, 1H), 4.84 (d, *J*=6.8 Hz, 1H), 4.81 (d, *J*=6.8 Hz, 1H), 4.56 (d, *J*=11.2 Hz, 1H), 4.55–4.50 (m, 3H), 4.04 (br dd, *J*=6.8, 6.8 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.56–3.34 (m, 6H), 3.27 (s, 3H), 3.24 (s, 3H), 3.20 (s, 3H), 2.42 (m, 1H), 2.35–2.18 (m, 4H), 2.18 (s, 3H), 2.10 (dd, *J*=7.3, 12.2 Hz, 1H), 1.86–1.00 (m, 19H), 1.10 (d, *J*=6.8 Hz, 3H), 0.95 (d, *J*=7.3 Hz, 3H), 0.93 (d, *J*=6.8 Hz, 3H), 0.92–0.85 (m, 6H), 0.90 (s, 9H), 0.89 (s, 9H), 0.87 (d, *J*=6.8 Hz, 3H), 0.77 (d, *J*=6.4 Hz, 3H), 0.12 (s, 3H), 0.05 (s, 6H), 0.04 (s, 3H); MS (FAB) *m/z* 1255 (M+Na)$^+$; HRMS (FAB) calcd for $C_{68}H_{120}NaO_{13}SSi_2$ [(M+Na)$^+$] 1255.7887, found 1255.7870.

3.1.15. Diol 25. To a stirred solution of disilyl ether **24** (28.5 mg, 0.0231 mmol) in 1,2-dimethoxyethane (3.2 mL) was added 1 M aqueous HCl (0.8 mL) at room temperature. The solution was stirred at room temperature for 6.5 h, cooled to 0°C, and diluted with saturated aqueous $NaHCO_3$ (2 mL). The mixture was extracted with Et_2O (3×10 mL). The combined extracts were washed with brine (3 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (4 g, hexane–EtOAc 5:1→3:1→3:2) to give a diastereomeric mixture of hemiacetals (19.7 mg) as a colorless oil along with recovered **24** (3.0 mg, 11%). To a stirred solution of the hemiacetals (19.7 mg) in MeOH (0.5 mL) cooled at 0°C was added sodium trimethoxyborohydride (22.8 mg, 0.178 mmol). The solution was stirred at room temperature for 4.5 h. The reaction was quenched by adding acetone (0.2 mL) and the resulting mixture was stirred at room temperature for 10 min. Et_2O (2 mL) and saturated aqueous NH_4Cl (1 mL) were added, and the mixture was stirred for 10 min and separated. The aqueous layer was extracted with Et_2O (3×10 mL). The organic layer and the extracts were combined, washed with brine (3 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (2 g, hexane–EtOAc 3:1→3:2→1:1→1:2) to give **25** (19.0 mg, 67%) as a colorless oil: $[\alpha]_D^{29}$=+13.4 (*c* 1.03, $CHCl_3$); IR ($CHCl_3$) 3420 (br), 1705, 1645, 1615, 1595, 1515, 1465, 1375, 1260, 1030, 970, 835 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (ddd, *J*=4.9, 10.3, 15.1 Hz, 1H), 7.00–6.87 (m, 2H), 6.83 (d, *J*=8.8 Hz, 1H), 6.25–6.16 (m, 2H), 5.81 (d, *J*=15.1 Hz, 1H), 5.53 (ddd, *J*=3.9, 10.2, 15.1 Hz, 1H), 5.33–5.23 (m, 2H), 5.14–5.07 (m, 2H), 4.82 (d, *J*=6.8 Hz, 1H), 4.77 (d, *J*=6.8 Hz, 1H), 4.65 (d, *J*=11.7 Hz, 1H), 4.60 (d, *J*=11.7 Hz, 1H), 4.55 (d, *J*=11.7 Hz, 1H), 4.53 (d, *J*=11.7 Hz, 1H), 4.06 (br s, 1H, –OH), 3.89 (s, 3H), 3.89 (m, 1H), 3.88 (s, 3H), 3.72 (ddd, *J*=5.4, 5.4, 11.7 Hz, 1H), 3.58–3.37 (m, 7H), 3.24 (s, 3H), 3.20 (s, 3H), 3.06 (br s, 1H, –OH), 2.45 (m, 1H), 2.34–2.16 (m, 3H), 2.17 (s, 3H), 1.94–1.69 (m, 6H), 1.67–1.09 (m, 15H), 1.02 (d, *J*=6.8 Hz, 3H), 0.95–0.88 (m, 6H), 0.95 (d, *J*=7.3 Hz, 3H), 0.93 (d, *J*=6.8 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.87 (d, *J*=5.6 Hz, 3H), 0.77 (d, *J*=6.3 Hz, 3H), 0.12 (s, 3H), 0.05 (s, 6H), 0.04 (s, 3H); MS (FAB) *m/z* 1243 (M+Na)$^+$; HRMS (FAB) calcd for $C_{67}H_{120}NaO_{13}SSi_2$ [(M+Na)$^+$] 1243.7886, found 1243.7880.

3.1.16. Silyl ether 26. To a stirred solution of diol **25** (9.3 mg, 7.6 μmol) in CH_2Cl_2 (0.1 mL) was added Et_3N (0.025 mL, 0.18 mmol), DMAP (0.7 mg, 5.7 μmol), and *t*-BuMe$_2$SiCl (18.0 mg, 0.119 mmol) at room temperature. The solution was stirred at room temperature for 35 min. Ice (ca. 1 g) and saturated aqueous $NaHCO_3$ (1 mL) were added and the mixture was stirred at room temperature for 30 min and extracted with Et_2O (3×5 mL). The combined extracts were washed with brine (2 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (2 g, hexane–EtOAc 4:1→3:1→2:1) to give **26** (10.2 mg, 100%) as a colorless oil: $[\alpha]_D^{30}$=+15.5 (*c* 0.55, $CHCl_3$); IR ($CHCl_3$) 3495, 1705, 1640, 1615, 1595, 1515, 1460, 1375, 1260, 1095, 1030, 970, 835 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (ddd, *J*=4.4, 9.8, 15.1 Hz, 1H), 6.89–6.87 (m, 2H), 6.83 (d, *J*=8.8 Hz, 1H), 6.25–6.15 (m, 2H), 5.80 (d, *J*=15.1 Hz, 1H), 5.54 (ddd, *J*=4.4, 10.7, 15.1 Hz, 1H), 5.33–5.25 (m, 2H), 5.14–5.06 (m, 2H), 4.82 (d, *J*=7.3 Hz, 1H), 4.76 (d, *J*=7.3 Hz, 1H), 4.64 (d, *J*=11.7 Hz, 1H), 4.60 (d, *J*=11.7 Hz, 1H), 4.56 (d, *J*=11.7 Hz, 1H), 4.53 (d, *J*=11.7 Hz, 1H), 3.89 (s, 3H), 3.88 (m, 1H), 3.87 (s, 3H), 3.74–3.39 (m, 9H), 3.24 (s, 3H), 3.20 (s, 3H), 2.45–2.17 (m, 4H), 2.17 (s, 3H), 1.87–1.15 (m, 21H), 1.00 (d, *J*=6.8 Hz, 3H), 0.94 (d, *J*=6.8 Hz, 3H), 0.92 (d, *J*=6.3 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 18H), 0.90–0.86 (m, 6H), 0.84 (d, *J*=6.8 Hz, 3H), 0.77 (d, *J*=6.3 Hz, 3H), 0.12 (s, 3H), 0.05 (s, 6H), 0.04 (s, 9H); MS (FAB) *m/z* 1357 (M+Na)$^+$; HRMS (FAB) calcd for $C_{73}H_{134}NaO_{13}SSi_3$ [(M+Na)$^+$] 1357.8751, found 1357.8770.

3.1.17. Acetate 27. To a stirred solution of silyl ether **26** (17.0 mg, 0.0124 mmol) in pyridine (0.2 mL) were added

Ac_2O (0.1 mL) and DMAP (0.7 mg, 5.7 μmol) at room temperature. The mixture was stirred at room temperature for 13 h and concentrated. The residual oil was purified by column chromatography on silica gel (2 g, hexane–EtOAc 5:1→4:1→3:1) to give **27** (16.7 mg, 95%) as a colorless oil: $[\alpha]_D^{30}$=+34 (*c* 0.20, $CHCl_3$); IR ($CHCl_3$) 1720, 1705, 1640, 1615, 1595, 1515, 1465, 1375, 1255, 1030, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.22 (ddd, *J*=4.4, 10.2, 15.1 Hz, 1H), 6.89–6.87 (m, 2H), 6.82 (d, *J*=7.8 Hz, 1H), 6.25–6.15 (m, 2H), 5.80 (d, *J*=15.1 Hz, 1H), 5.53 (ddd, *J*=4.4, 10.2, 15.1 Hz, 1H), 5.33–5.24 (m, 2H), 5.14–5.06 (m, 2H), 5.00 (dd, *J*=2.4, 9.8 Hz, 1H), 4.77 (d, *J*=6.8 Hz, 1H), 4.67 (d, *J*=6.8 Hz, 1H), 4.62 (d, *J*=11.7 Hz, 1H), 4.60 (d, *J*=11.7 Hz, 1H), 4.55 (d, *J*=11.7 Hz, 1H), 4.49 (d, *J*=11.7 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.69 (m, 1H), 3.60–3.39 (m, 7H), 3.24 (s, 3H), 3.20 (s, 3H), 2.47 (m, 1H), 2.36–2.17 (m, 3H), 2.17 (s, 3H), 2.03 (s, 3H), 2.03–1.17 (m, 21H), 0.93 (d, *J*=6.8 Hz, 3H), 0.93–0.86 (m, 12H), 0.90 (s, 9H), 0.89 (s, 9H), 0.89 (s, 9H), 0.87 (d, *J*=6.3 Hz, 3H), 0.77 (d, *J*=5.9 Hz, 3H), 0.13 (s, 3H), 0.06 (s, 3H), 0.05 (s, 12H); MS (FAB) *m/z* 1399 $(M+Na)^+$; HRMS (FAB) calcd for $C_{75}H_{136}NaO_{14}SSi_3$ [$(M+Na)^+$] 1399.8856, found 1399.8850.

3.1.18. Alcohol 28. To a stirred solution of acetate **27** (8.0 mg, 5.8 μmol) in CH_2Cl_2 (1.8 mL), *tert*-butyl alcohol (0.1 mL), and 1 M phosphate buffer (pH 6, 0.1 mL) cooled at 0°C was added 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) (2.0 mg, 8.8 μmol). The mixture was warmed to room temperature and stirred for 30 min. The mixture was diluted with 1 M phosphate buffer (pH 6, 2 mL), stirred at room temperature for 40 min, and extracted with Et_2O (10 mL, 3×3 mL). The combined extracts were successively washed with 1 M phosphate buffer (pH 6, 2 mL), saturated aqueous $NaHCO_3$ (2 mL), H_2O (2 mL), and brine (2 mL), and then dried (Na_2SO_4) and concentrated. The residual oil was purified by preparative TLC on silica gel (200×100×0.25 mm^3, hexane–acetone 3:1) to give **28** (6.0 mg, 86%) as a colorless oil: $[\alpha]_D^{30}$=+29 (*c* 0.21, $CHCl_3$); IR ($CHCl_3$) 3520 (br), 1705, 1655, 1465, 1375, 1255, 1080, 1050, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (m, 1H), 6.25–6.16 (m, 2H), 5.81 (d, *J*=15.1 Hz, 1H), 5.54 (ddd, *J*=4.4, 10.3, 15.1 Hz, 1H), 5.33–5.26 (m, 2H), 5.14–5.06 (m, 2H), 4.81 (dd, *J*=2.4, 10.4 Hz, 1H), 4.61 (d, *J*=11.7 Hz, 1H), 4.56 (d, *J*=11.7 Hz, 1H), 3.71 (ddd, *J*=3.9, 6.3, 10.2 Hz, 1H), 3.62–3.54 (m, 3H), 3.50 (ddd, *J*=4.9, 4.9, 8.8 Hz, 1H), 3.45–3.38 (m, 3H), 3.24 (s, 3H), 3.20 (s, 3H), 2.62 (d, *J*=3.4 Hz, 1H), 2.45 (m, 1H), 2.37–2.01 (m, 4H), 2.18 (s, 3H), 2.12 (s, 3H), 1.89–1.17 (m, 20H), 0.97–0.84 (m, 9H), 0.96 (d, *J*=7.3 Hz, 3H), 0.93 (d, *J*=6.8 Hz, 3H), 0.90 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.85 (d, *J*=6.8 Hz, 3H), 0.77 (d, *J*=6.3 Hz, 3H), 0.12 (s, 3H), 0.05 (s, 9H), 0.04 (s, 6H); MS (FAB) *m/z* 1219 $(M+Na)^+$; HRMS (FAB) calcd for $C_{65}H_{124}NaO_{11}SSi_3$ [$(M+Na)^+$] 1219.8070, found 1219.8090.

3.1.19. Dimethylalanine ester 29. To a mixture of alcohol **28** (4.4 mg, 3.7 μmol), L-*N*,*N*-dimethylalanine (3.9 mg, 0.033 mmol), D-*N*,*N*-dimethylalanine (2.8 mg, 0.024 mmol), DMAP (20.9 mg, 0.17 mmol), and (±)-camphorsulfonic acid (15.2 mg, 0.065 mmol) was added a 0.22 M solution of DCC in CH_2Cl_2 (0.26 mL, 0.057 mmol) at room temperature. The mixture was stirred at room temperature for 12 h, and saturated aqueous $NaHCO_3$ (2.5 mL) was added. The mixture was stirred at room temperature for 30 min and extracted with EtOAc (3×10 mL). The combined extracts were washed with brine (2 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (2 g, hexane–acetone 10:1→7:1→ 5:1) and preparative TLC on silica gel (200×100× 0.25 mm^3, hexane–acetone 2:1) to give a diastereomeric mixture of **29** (*S*/*R*=3:1) (4.8 mg, 100%) as a colorless oil: $[\alpha]_D^{30}$=+31 (*c* 0.17, MeOH); IR ($CHCl_3$) 1725, 1700, 1655, 1465, 1375, 1250, 1080, 1035, 970, 835 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.25 (dd, *J*=10.7, 15.1 Hz, 1H), 6.44–6.27 (m, 2H), 5.90 (d, *J*=15.1 Hz, 1H), 5.56 (ddd, *J*=4.4, 10.7, 14.6 Hz, 1H), 5.38 (ddd, *J*=5.4, 8.8, 14.6 Hz, 1H), 5.32 (ddd, *J*=2.0, 4.9, 10.7 Hz, 1H), 5.09 (dd, *J*=8.8, 14.6 Hz, 1H), 5.06 (dd, *J*=8.8, 14.6 Hz, 1H), 4.95 (br dd, *J*=6.3, 6.3 Hz, 1H), 4.81 (dd, *J*=2.4, 9.8 Hz, 1H), 4.69 (d, *J*=11.7 Hz, 1H), 4.65 (d, *J*=11.7 Hz, 1H), 3.76–3.43 (m, 6H), 3.55 (dd, *J*=4.9, 4.9 Hz, 1H), 3.18 (m, 3H), 3.18 (s, 3H), 3.12 (s, 3H), 2.51 (m, 1H), 2.41 [2.37] (s, 6H), 2.41–2.25 (m, 3H), 2.18 (s, 3H), 2.02–1.09 (m, 24H), 0.99 (d, *J*=6.8 Hz, 3H), 0.99 (d, *J*=6.8 Hz, 3H), 0.98–0.87 (m, 9H), 0.94 (s, 9H), 0.91 (s, 9H), 0.90 (s, 9H), 0.87 (d, *J*=6.8 Hz, 3H), 0.78 (d, *J*=6.3 Hz, 3H), 0.17 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.07 (s, 3H). Signals of three protons (CH_3COO) were overlapped with the solvent signals. The minor counterparts of doubled signals in the ratio of 3:1 are in brackets; MS (FAB) *m/z* 1318 $(M+Na)^+$; HRMS (FAB) calcd for $C_{70}H_{133}NNaO_{12}SSi_3$ [$(M+Na)^+$] 1318.8753, found 1318.8710.

3.1.20. Alcohol 30. To a stirred solution of dimethylalanine ester **29** (*S*/*R*=3:1) (3.5 mg, 2.7 μmol) in THF (0.20 mL) and H_2O (0.05 mL) were added 2,6-lutidine (0.05 mL, 0.43 mmol) and $AgNO_3$ (69 mg, 0.41 mmol) at room temperature. The mixture was stirred at 30°C for 22 h in the dark and filtered through a pad of Celite, and the residue was washed with EtOAc (20 mL). The filtrate and the washings were combined, washed with H_2O (4 mL) and brine (4 mL), and concentrated. The residual oil was purified by column chromatography on silica gel (2 g, hexane–acetone 5:1→4:1) to give **30** (*S*/*R*=3:1) (2.8 mg, 80%) as a colorless oil: $[\alpha]_D^{29}$=+23 (*c* 0.13, MeOH); IR ($CHCl_3$) 3450 (br), 1725, 1705, 1640, 1460, 1360, 1250, 1080, 1035, 970, 835 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.24 (m, 1H), 6.41–6.32 (m, 2H), 5.87 (d, *J*=15.1 Hz, 1H), 5.56 (ddd, *J*=4.4, 10.7, 15.1 Hz, 1H), 5.40 (ddd, *J*=5.9, 10.7, 15.1 Hz, 1H), 5.31 (ddd, *J*=2.0, 4.9, 10.7 Hz, 1H), 5.12–5.04 (m, 2H), 4.94 (m, 1H), 4.80 (dd, *J*=2.4, 10.3 Hz, 1H), 3.85–3.60 (m, 5H), 3.55 (dd, *J*=4.4, 4.4 Hz, 1H), 3.51–3.44 (m, 2H), 3.18 (m, 1H), 3.17 (s, 3H), 3.12 (s, 3H), 2.52 (m, 1H), 2.40–2.21 (m, 3H), 2.32 [2.30] (s, 6H), 2.00 (s, 3H), 1.95–1.06 (m, 21H), 1.24 [1.20] (d, *J*=7.8 Hz, 3H), 0.99 (d, *J*=6.8 Hz, 3H), 0.99 (d, *J*=6.8 Hz, 3H), 0.96–0.87 (m, 9H), 0.94 (s, 9H), 0.91 (s, 9H), 0.90 (s, 9H), 0.88 (d, *J*=6.8 Hz, 3H), 0.78 (d, *J*=6.3 Hz, 3H), 0.16 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H). Signals of three protons (CH_3COO) were overlapped with the solvent signals. The minor counterparts of doubled signals in the ratio of 3:1 are in brackets; MS (FAB) *m/z* 1258 $(M+Na)^+$; HRMS (FAB) calcd for $C_{68}H_{129}NNaO_{12}Si_3$ [$(M+Na)^+$] 1258.8721, found 1258.8760.

3.1.21. Trimethylserine ester 31. To a mixture of alcohol **30** (*S*/*R*=3:1) (2.8 mg, 2.3 μmol), L-*N*,*N*,*O*-trimethylserine (7.0 mg, 0.048 mmol), D-*N*,*N*,*O*-trimethylserine (2.4 mg, 0.018 mmol), DMAP (21.7 mg, 0.178 mmol), and (±)-camphorsulfonic acid (15.4 mg, 0.066 mmol) was added a 0.15 M solution of DCC in CH_2Cl_2 (0.40 mL, 0.060 mmol) at room temperature. The mixture was stirred at 35°C for 1.5 h, cooled to room temperature, and diluted with saturated aqueous $NaHCO_3$ (2 mL). The mixture was stirred at room temperature for 40 min and extracted with EtOAc (3×10 mL). The combined extracts were washed with brine (3 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (2 g, hexane–acetone 5:1→4:1→3:1) and preparative TLC on silica gel (200×100×0.25 mm^3, hexane–EtOAc 1:4; 200×100×0.25 mm^3, benzene–EtOAc 1:1) to give a diastereomeric mixture of **31** (*S*/*R*=4:3 as to the trimethylserine part, *S*/*R*=3:1 as to the dimethylalanine part) (2.2 mg, 72%) as a colorless amorphous powder: $[\alpha]_D^{29}$=+2.5 (*c* 0.12, MeOH); IR ($CHCl_3$) 1730, 1700 1655, 1460, 1375, 1250, 1095, 970, 835 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.21 [7.22][b] (dd, *J*=10.7, 15.1 Hz, 1H), 6.40 [6.41][b] (dd, *J*=10.7, 15.1 Hz, 1H), 6.27 (m, 1H), 5.91 (d, *J*=15.1 Hz, 1H), 5.56 (ddd, *J*=4.4, 10.7, 15.1 Hz, 1H), 5.41–5.30 (m, 2H), 5.13 (dd, *J*=8.8, 15.1 Hz, 1H), 5.07 (dd, *J*=8.8, 15.1 Hz, 1H), 4.94 (m, 1H), 4.86 (m, 1H), 4.80 (dd, *J*=2.4, 10.3 Hz, 1H), 3.78–3.56 (m, 6H), 3.54 (dd, *J*=4.4, 4.4 Hz, 1H), 3.51–3.48 (m, 2H), 3.38 (ddd, *J*=2.4, 5.4, 8.3 Hz, 1H), 3.33 [3.31][b] (s, 3H), 3.19 (m, 1H), 3.18 (s, 3H), 3.12 (s, 3H), 2.59–2.52 (m, 2H), 2.39–2.13 (m, 3H), 2.36 [2.36][b] (s, 6H), 2.32 [2.29][a] (s, 6H), 1.99–1.06 (m, 19H), 1.24 [1.20][a] (d, *J*=7.3 Hz, 3H), 1.00–0.87 (m, 12H), 0.99 (d, *J*=6.8 Hz, 3H), 0.94 (s, 9H), 0.91 (s, 9H), 0.90 (s, 9H), 0.87 (d, *J*=6.8 Hz, 3H), 0.78 (d, *J*=6.8 Hz, 3H), 0.16 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.06 (s, 6H). Signals of three protons (CH_3COO) were overlapped with the solvent signals. The minor counterparts of doubled signals in the ratios of 3:1 (superscript a) and 4:3 (superscript b) are in brackets; MS (FAB) *m*/*z* 1387 $(M+Na)^+$; HRMS (FAB) calcd for $C_{74}H_{140}N_2NaO_{14}Si_3$ $[(M+Na)^+]$ 1387.9509, found 1387.9510.

3.1.22. Analog 32. A solution of trimethylserine ester **31** (*S*/*R*=4:3 as to the trimethylserine part, *S*/*R*=3:1 as to the dimethylalanine part) (2.0 mg, 1.5 μmol) in a 5:3:8 mixture of HF·pyridine, pyridine, and THF (0.5 mL) was stirred at room temperature for 22 h. The mixture was diluted with EtOAc (2 mL) and poured into saturated aqueous $NaHCO_3$ (4 mL) cooled at 0°C, and the resulting mixture was extracted with EtOAc (3×10 mL). The combined extracts were washed with brine (2 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (0.4 g, hexane–EtOAc–MeOH 4:4:1→1:1:1) and HPLC (Develosil 60-5, 10×250 mm^2, hexane–EtOAc–MeOH 4:4:1, flow rate 2.5 mL/min) to give **32** (*S*/*R*=4:3 as to the trimethylserine part, *S*/*R*=3:1 as to the dimethylalanine part) (1.0 mg, 80%) as a colorless amorphous powder: $[\alpha]_D^{30}$=+53 (*c* 0.051, MeOH); UV (MeCN) λ_{max} 261 nm (ε 29,000); IR ($CHCl_3$) 3490 (br), 1725, 1700, 1640, 1620, 1600, 1460, 1370, 1245, 1090, 970 cm^{-1}; ^1H NMR (600 MHz, acetone-d_6) δ 7.21 [7.22][b] (dd, *J*=11.0, 15.0 Hz, 1H), 6.44 [6.45][b] (dd, *J*=11.0, 15.0 Hz, 1H), 6.29 (m, 1H), 5.97 [5.98][b] (d, *J*=15.0 Hz, 1H), 5.62 (ddd, *J*=4.4, 11.0, 15.0 Hz, 1H), 5.47 (br d, *J*=11.0 Hz, 1H), 5.18 (m, 1H), 5.10 (ddd, *J*=5.1, 8.8, 13.9 Hz, 1H), 4.99 (dd, *J*=8.8, 15.0 Hz, 1H), 4.96 (m, 1H), 4.78 (dd, *J*=2.6, 9.9 Hz, 1H), 4.76 (m, 1H), 3.68 (dd, *J*=7.7, 9.2 Hz, 1H), 3.64 (m, 1H), 3.60–3.57 (m, 2H), 3.55–3.45 (m, 4H), 3.37 (ddd, *J*=5.5, 5.5, 7.3 Hz, 1H), 3.33 [3.30][b] (s, 3H), 3.30 (m, 1H), 3.18 (m, 1H), 3.18 (s, 3H), 3.10 (s, 3H), 3.05 (m, 1H), 2.49–2.41 (m, 3H), 2.35 [2.36][b] (s, 6H), 2.32 [2.30][a] (s, 6H), 2.30 (m, 1H), 2.15 (m, 1H), 1.99 [1.97][a] (s, 3H), 1.88 (m, 1H), 1.79–1.13 (m, 20H), 1.24 [1.19][a] (d, *J*=7.0 Hz, 3H), 1.02–0.98 (m, 12H), 0.91 (d, *J*=7.0 Hz, 3H), 0.87 (d, *J*=7.0 Hz, 3H), 0.73 [0.72][b] (d, *J*=7.0 Hz, 3H). The minor counterparts of doubled signals in the ratios of 3:1 (superscript a), and 4:3 (superscript b) are in brackets; MS (FAB) *m*/*z* 1045 $(M+Na)^+$; HRMS (FAB) calcd for $C_{56}H_{98}N_2NaO_{14}$ $[(M+Na)^+]$ 1045.6916, found 1045.6930.

3.1.23. Alcohol 33. The experimental procedure was similar to that described for compound **30**. **33** (84% yield): a colorless oil; $[\alpha]_D^{27}$=+37 (*c* 0.15, $CHCl_3$); IR ($CHCl_3$) 3450 (br), 1725, 1705, 1640, 1460, 1375, 1250, 1100, 1035, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, *J*=11.0, 15.0 Hz, 1H), 6.90–6.87 (m, 2H), 6.82 (d, *J*=7.8 Hz, 1H), 6.31–6.17 (m, 2H), 5.78 (d, *J*=15.1 Hz, 1H), 5.50 (ddd, *J*=4.4, 10.3, 15.1 Hz, 1H), 5.40 (ddd, *J*=6.8, 6.8, 15.1 Hz, 1H), 5.26–5.12 (m, 3H), 5.00 (dd, *J*=2.4, 9.8 Hz, 1H), 4.77 (d, *J*=6.8 Hz, 1H), 4.67 (d, *J*=6.8 Hz, 1H), 4.62 (d, *J*=11.7 Hz, 1H), 4.49 (d, *J*=11.7 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.77 (m, 1H), 3.69 (m, 1H), 3.60–3.38 (m, 7H), 3.23 (s, 3H), 3.21 (m, 1H, –OH), 3.20 (s, 3H), 2.48 (m, 1H), 2.35–2.17 (m, 3H), 2.05–1.94 (m, 2H), 2.03 (s, 3H), 1.92–1.00 (m, 18H), 0.95 (d, *J*=6.8 Hz, 3H), 0.93 (d, *J*=6.8 Hz, 3H), 0.93–0.88 (m, 9H), 0.91 (br s, 18H), 0.89 (s, 9H), 0.85 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.3 Hz, 3H), 0.13 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 6H); MS (FAB) *m*/*z* 1339 $(M+Na)^+$; HRMS (FAB) calcd for $C_{73}H_{132}NaO_{14}Si_3$ $[(M+Na)^+]$ 1339.8823, found 1339.8800.

3.1.24. Trimethylserine ester 34. The experimental procedure was similar to that described for compound **31**. **34** (88% yield, *S*/*R*=4:3): a colorless amorphous powder; $[\alpha]_D^{29}$=+20 (*c* 0.096, MeOH); IR ($CHCl_3$) 1730, 1700, 1655, 1460, 1375, 1250, 1095, 970, 835 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.20 [7.21] (dd, *J*=10.7, 15.1 Hz, 1H), 6.94–6.85 (m, 3H), 6.39 [6.39] (dd, *J*=10.7, 15.1 Hz, 1H), 6.24 (m, 1H), 5.90 (d, *J*=15.1 Hz, 1H), 5.55 (ddd, *J*=4.4, 10.7, 15.1 Hz, 1H), 5.37 (m, 1H), 5.30 (dd, *J*=4.4, 10.7 Hz, 1H), 5.12 (dd, *J*=8.8, 15.1 Hz, 1H), 5.06 (dd, *J*=8.8, 15.1 Hz, 1H), 4.99 (dd, *J*=2.4, 10.3 Hz, 1H), 4.85 [4.86] (dd, *J*=6.8, 6.8 Hz, 1H), 4.74 (d, *J*=6.8 Hz, 1H), 4.65 (d, *J*=6.8 Hz, 1H), 4.60 (d, *J*=11.7 Hz, 1H), 4.45 (d, *J*=11.7 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.76–3.56 (m, 6H), 3.52 (dd, *J*=4.9, 4.9 Hz, 1H), 3.51–3.43 (m, 2H), 3.38 (ddd, *J*=2.0, 5.4, 7.8 Hz, 1H), 3.33 [3.30] (s, 3H), 3.18 (s, 3H), 3.12 (s, 3H), 2.56–2.45 (m, 2H), 2.43–1.03 (m, 23H), 2.36 [2.36] (s, 6H), 2.08 (s, 3H), 0.98–0.89 (m, 12H), 0.97 (d, *J*=6.8 Hz, 3H), 0.93 (s, 9H), 0.91 (s, 9H), 0.90 (s, 9H), 0.78 (d, *J*=7.3 Hz, 3H), 0.88 (d, *J*=6.3 Hz, 3H), 0.16 (s, 3H), 0.11 (s, 3H), 0.09 [0.08] (s, 3H), 0.07 (s, 3H), 0.06 (s, 6H). The minor counterparts of doubled signals in the ratio of 4:3 are in brackets; MS (FAB) *m*/*z* 1468 $(M+Na)^+$; HRMS (FAB) calcd for $C_{79}H_{143}NNaO_{16}Si_3$ $[(M+Na)^+]$ 1468.9612, found 1468.9560.

3.1.25. Alcohol 35. The experimental procedure was similar to that described for compound **32**. **35** (98% yield, *S*/*R*=4:3): a colorless oil; $[\alpha]_D^{28}$=+52 (*c* 0.054, MeOH); IR ($CHCl_3$) 3480 (br), 1730, 1690, 1655, 1455, 1370, 1240, 1080, 970 cm^{-1}; ^1H NMR (600 MHz, acetone-d_6) δ 7.21 (dd, *J*=10.7, 15.1 Hz, 1H), 6.95–6.86 (m, 3H), 6.44 [6.45] (dd, *J*=10.7, 15.1 Hz, 1H), 6.29 (m, 1H), 5.97 (d, *J*=15.1 Hz, 1H), 5.59 (ddd, *J*=4.4, 10.7, 15.1 Hz, 1H), 5.45–5.34 (m, 2H), 5.10 (m, 1H), 5.00–4.95 (m, 2H), 4.76 (m, 1H), 4.75 (d, *J*=6.8 Hz, 1H), 4.67 (d, *J*=6.8 Hz, 1H), 4.62 (d, *J*=11.7 Hz, 1H), 4.44 (d, *J*=11.7 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.70–3.45 (m, 9H), 3.39–3.30 (m, 2H), 3.33 [3.30] (s, 3H), 3.18 (s, 3H), 3.10 (s, 3H), 3.03 (m, 1H), 2.50–2.35 (m, 2H), 2.36 [2.35] (s, 6H), 2.30–1.85 (m, 10H), 1.77–0.97 (m, 26H), 0.90 (d, *J*=6.8 Hz, 3H), 0.89 (d, *J*=6.8 Hz, 3H), 0.87 (d, *J*=6.8 Hz, 3H), 0.73 [0.71] (d, *J*=6.3 Hz, 3H). The minor counterparts of doubled signals in the ratio of 4:3 are in brackets; MS (FAB) *m*/*z* 1126 $(M+Na)^+$; HRMS (FAB) calcd for $C_{61}H_{101}NNaO_{16}$ $[(M+Na)^+]$ 1126.7018, found 1126.7020.

3.1.26. Analog 36. The experimental procedure was similar to that described for compound **28**. **36** (86% yield, *S*/*R*=4:3): a colorless amorphous powder: $[\alpha]_D^{30}$=+57 (*c* 0.058, MeOH); UV (MeCN) λ_{max} 262 nm (ε 28,000); IR ($CHCl_3$) 3500 (br), 1710, 1640, 1620, 1560, 1460, 1370, 1260, 1140, 1090, 970 cm^{-1}; ^1H NMR (600 MHz, acetone-d_6) δ 7.21 (dd, *J*=11.0, 15.0 Hz, 1H), 6.44 [6.45] (dd, *J*=11.0, 15.0 Hz, 1H), 6.29 (m, 1H), 5.97 [5.98] (d, *J*=15.0 Hz, 1H), 5.61 (ddd, *J*=4.0, 11.0, 15.0 Hz, 1H), 5.47 [5.47] (d, *J*=11.0 Hz, 1H), 5.38 (m, 1H), 5.10 [5.10] (ddd, *J*=5.1, 9.2, 15.0 Hz, 1H), 4.99 (dd, *J*=9.2, 15.0 Hz, 1H), 4.86 (dd, *J*=2.6, 9.9 Hz, 1H), 4.76 (m, 1H), 3.68 (dd, *J*=7.7, 8.8 Hz, 1H), 3.66 (m, 1H), 3.58 [3.58] (dd, *J*=5.5, 9.2 Hz, 1H), 3.54–3.42 (m, 7H), 3.37 (ddd, *J*=5.5, 5.5, 7.7 Hz, 1H), 3.33 [3.30] (s, 3H), 3.28 (m, 1H), 3.18 [3.18] (s, 3H), 3.10 (s, 3H), 3.04 (m, 1H), 3.00 (d, *J*=4.4 Hz, 1H), 2.49–2.41 (m, 2H), 2.35 [2.36] (s, 6H), 2.33 (m, 1H), 2.14 (m, 1H), 2.06 [2.08] (s, 3H), 1.99 (m, 1H), 1.90–1.04 (m, 20H), 1.00 [1.02] (d, *J*=6.6 Hz, 3H), 1.00 (d, *J*=6.6 Hz, 3H), 0.97 (d, *J*=6.6 Hz, 3H), 0.89 (d, *J*=6.6 Hz, 3H), 0.89 (d, *J*=6.6 Hz, 3H), 0.85 (d, *J*=7.0 Hz, 3H), 0.73 [0.72] (d, *J*=7.0 Hz, 3H). The minor counterparts of doubled signals in the ratio of 4:3 are in brackets; MS (FAB) *m*/*z* 946 $(M+Na)^+$; HRMS (FAB) calcd for $C_{51}H_{89}NNaO_{13}$ $[(M+Na)^+]$ 946.6232, found 946.6231.

3.1.27. TES ether 37. To a mixture of silyl ether **26** (7.0 mg, 5.25 μmol), imidazole (7.6 mg, 0.12 mmol) in DMF (0.2 mL) was added Et_3SiCl (9 μL, 0.054 mmol). After being stirred at room temperature for 3 h, the mixture was diluted with ice (1 g) and saturated aqueous $NaHCO_3$ and extracted with Et_2O (3×10 mL). The combined extracts were washed with brine (2 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (2 g, hexane–Et_2O 4:1→3:1→2:1→1:1→1:2) to give **31** (7.7 mg, 100%) as a colorless oil: $[\alpha]_D^{29}$=+29 (*c* 0.41, $CHCl_3$); IR ($CHCl_3$) 1705, 1645, 1615, 1595, 1515, 1465, 1375, 1255, 1095, 1030, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.22 (m, 1H), 6.89–6.87 (m, 2H), 6.83 (d, *J*=8.3 Hz, 1H), 6.25–6.14 (m, 2H), 5.80 (d, *J*=15.1 Hz, 1H), 5.54 (ddd, *J*=4.4, 10.3, 15.1 Hz, 1H), 5.33–5.26 (m, 2H), 5.14–5.06 (m, 2H), 4.78 (s, 2H), 4.61 (d, *J*=11.7 Hz, 1H), 4.60 (d, *J*=11.7 Hz, 1H), 4.55 (d, *J*=11.7 Hz, 1H), 4.50 (d, *J*=11.7 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.75 (br dd, *J*=5.9, 5.9 Hz, 1H), 3.68 (ddd, *J*=4.4, 6.8, 11.2 Hz, 1H), 3.60–3.39 (m, 7H), 3.24 (s, 3H), 3.20 (s, 3H), 2.45 (m, 1H), 2.34–2.17 (m, 3H), 2.17 (s, 3H), 1.89–1.09 (m, 21H), 0.96–0.77 (m, 12H), 0.94 (t, *J*=7.8 Hz, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.89 (s, 9H), 0.87 (d, *J*=6.8 Hz, 3H), 0.86 (d, *J*=7.3 Hz, 3H), 0.77 (d, *J*=6.3 Hz, 3H), 0.61 (q, *J*=7.8 Hz, 6H), 0.12 (s, 3H), 0.05 (s, 6H), 0.05 (s, 9H); MS (FAB) *m*/*z* 1471 $(M+Na)^+$; HRMS (FAB) calcd for $C_{79}H_{148}NaO_{13}SSi_4$ $[(M+Na)^+]$ 1471.9616, found 1471.9650.

3.1.28. Alcohol 38. The experimental procedure was similar to that described for compound **30**. **38** (54% yield): a colorless oil; $[\alpha]_D^{29}$=+47 (*c* 0.35, $CHCl_3$); IR ($CHCl_3$) 3450 (br), 1705, 1640, 1460, 1380, 1260, 1090, 1035, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, *J*=9.8, 15.1 Hz, 1H), 6.89–6.87 (m, 2H), 6.83 (d, *J*=7.8 Hz, 1H), 6.31–6.17 (m, 2H), 5.88 (d, *J*=15.1 Hz, 1H), 5.51 (ddd, *J*=3.9, 10.2, 15.1 Hz, 1H), 5.31 (m, 1H), 5.26–5.18 (m, 2H), 5.14 (dd, *J*=8.8, 15.1 Hz, 1H), 4.78 (s, 2H), 4.55 (d, *J*=11.7 Hz, 1H), 4.45 (d, *J*=11.7 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.77–3.43 (m, 9H), 3.23 (s, 3H), 3.20 (s, 3H), 3.14 (m, 1H, –OH), 2.46 (m, 1H), 2.35–2.17 (m, 3H), 2.01 (m, 1H), 1.81–1.05 (m, 20H), 0.96–0.89 (m, 12H), 0.94 (t, *J*=7.8 Hz, 9H), 0.91 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.86 (d, *J*=6.8 Hz, 3H), 0.85 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.8 Hz, 3H), 0.61 (q, *J*=7.8 Hz, 6H), 0.12 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 6H); MS (FAB) *m*/*z* 1411 $(M+Na)^+$; HRMS (FAB) calcd for $C_{77}H_{144}NaO_{13}Si_4$ $[(M+Na)^+]$ 1411.9581, found 1411.9530.

3.1.29. Trimethylserine ester 39. The experimental procedure was similar to that described for compound **31**. **39** (88% yield, *S*/*R*=4:3): a colorless oil; $[\alpha]_D^{30}$=+19 (*c* 0.31, MeOH); IR ($CHCl_3$) 1730, 1700, 1645, 1460, 1375, 1260, 1095, 970, 835 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.21 [7.21] (dd, *J*=10.7, 15.1 Hz, 1H), 6.94–6.86 (m, 3H), 6.38 [6.39] (dd, *J*=10.7, 15.1 Hz, 1H), 6.25 (m, 1H), 5.90 (d, *J*=15.1 Hz, 1H), 5.55 (ddd, *J*=4.4, 10.7, 15.1 Hz, 1H), 5.38 (m, 1H), 5.30 (m, 1H), 5.12 (dd, *J*=8.8, 15.1 Hz, 1H), 5.06 (dd, *J*=8.8, 15.1 Hz, 1H), 4.86 (ddd, *J*=2.4, 6.8, 6.8 Hz, 1H), 4.80 (s, 2H), 4.60 (d, *J*=11.7 Hz, 1H), 4.50 (d, *J*=11.7 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.76–3.52 (m, 8H), 3.48 (m, 2H), 3.38 (ddd, *J*=2.4, 5.4, 7.8 Hz, 1H), 3.33 [3.30] (s, 3H), 3.18 (s, 3H), 3.12 (s, 3H), 2.52–2.19 (m, 4H), 2.36 [2.36] (s, 6H), 2.00–1.06 (m, 21H), 0.99–0.88 (m, 18H), 0.97 (t, *J*=7.8 Hz, 9H), 0.93 (s, 9H), 0.91 (s, 9H), 0.90 (s, 9H), 0.78 (d, *J*=6.3 Hz, 3H), 0.67 (q, *J*=7.8 Hz, 6H), 0.16 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.06 (s, 6H). The minor counterparts of doubled signals in the ratio of 4:3 are in brackets; MS (FAB) *m*/*z* 1540 $(M+Na)^+$.

3.1.30. Analog 40. A solution of trimethylserine ester **39** (3.0 mg, 2.0 mmol) in 1,4-dioxane (0.6 mL) and 2 M HCl (0.2 mL) was stirred at 50°C for 2.5 h, diluted with EtOAc (10 mL) and saturated aqueous $NaHCO_3$ (5 mL), and extracted with EtOAc (3×10 mL). The combined extracts were washed with brine (2 mL), dried (Na_2SO_4), and concentrated. The residue was purified by preparative TLC on silica gel (200×100×0.25 mm^3, hexane–EtOAc–MeOH 2:2:1) to give **40** (1.0 mg, 57%, *S*/*R*=4:3) as a

colorless amorphous powder: $[\alpha]_D^{30}=+51$ (*c* 0.015, MeOH); UV (MeCN) λ_{max} 261 nm (ε 26,000); IR ($CHCl_3$) 3500 (br), 1710, 1640, 1620, 1560, 1460, 1370, 1260, 1140, 1090, 970 cm^{-1}; ^1H NMR (600 MHz, acetone-d_6) δ 7.21 [7.21] (dd, *J*=11.0, 15.4 Hz, 1H), 6.44 [6.45] (dd, *J*=11.0, 15.4 Hz, 1H), 6.29 (m, 1H), 5.97 [5.98] (d, *J*=15.4 Hz, 1H), 5.61 (ddd, *J*=4.0, 11.0, 15.0 Hz, 1H), 5.47 [5.47] (d, *J*=11.0 Hz, 1H), 5.38 (m, 1H), 5.09 [5.09] (ddd, *J*=5.5, 9.2, 15.0 Hz, 1H), 4.99 (dd, *J*=9.2, 15.0 Hz, 1H), 4.76 (m, 1H), 4.37 (d, *J*=5.5 Hz, 1H), 3.92 (m, 1H), 3.83 (d, *J*=4.0 Hz, 1H), 3.74–3.67 (m, 3H), 3.60–3.45 (m, 5H), 3.58 [3.58] (dd, *J*=5.5, 9.2 Hz, 1H), 3.39–3.30 (m, 3H), 3.33 [3.30] (s, 3H), 3.18 [3.18] (s, 3H), 3.10 (s, 3H), 3.05 (m, 1H), 2.49–2.29 (m, 3H), 2.35 [2.36] (s, 6H), 2.15 (m, 1H), 2.08–1.06 (m, 21H), 1.00 [1.02] (d, *J*=7.0 Hz, 3H), 1.00 (d, *J*=6.6 Hz, 3H), 0.97 (d, *J*=7.0 Hz, 3H), 0.91 (d, *J*=7.0 Hz, 3H), 0.91 (d, *J*=7.0 Hz, 3H), 0.90 (d, *J*=7.0 Hz, 3H), 0.73 [0.72] (d, *J*=6.6 Hz, 3H). The minor counterparts of doubled signals in the ratio of 4:3 are in brackets; MS (FAB) *m/z* 904 $(M+Na)^+$; HRMS (FAB) calcd for $C_{49}H_{87}NNaO_{12}$ $[(M+Na)^+]$ 904.6126, found 904.6125.

3.1.31. Alcohol 41. The experimental procedure was similar to that described for compound **30**. **41** (74% yield): a colorless oil: $[\alpha]_D^{29}=+38$ (*c* 0.29, $CHCl_3$); IR ($CHCl_3$) 3480 (br), 1710, 1640, 1460, 1375, 1255, 1100, 1050, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (m, 1H), 6.31–6.18 (m, 2H), 5.78 (d, *J*=15.1 Hz, 1H), 5.51 (ddd, *J*=4.4, 10.7, 15.1 Hz, 1H), 5.40 (m, 1H), 5.28–5.18 (m, 2H), 5.14 (dd, *J*=10.7, 15.1 Hz, 1H), 4.81 (dd, *J*=2.4, 10.7 Hz, 1H), 3.77 (m, 1H), 3.71 (ddd, *J*=3.9, 6.8, 10.7, Hz, 1H), 3.62–3.43 (m, 6H), 3.23 (s, 3H), 3.20 (s, 3H), 3.14 (br s, 1H, –OH), 2.61 (d, *J*=3.9 Hz, 1H, –OH), 2.46 (m, 1H), 2.32–2.21 (m, 3H), 2.12 (s, 3H), 2.05–1.97 (m, 2H), 1.83–1.05 (m, 19H), 0.96 (d, *J*=6.8 Hz, 3H), 0.95 (d, *J*=6.8 Hz, 3H), 0.92–0.90 (m, 6H), 0.91 (s, 9H), 0.90 (s, 9H), 0.90 (s, 9H), 0.86 (d, *J*=6.8 Hz, 3H), 0.85 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.8 Hz, 3H), 0.12 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.05 (s, 9H).; MS (FAB) *m/z* 1159 $(M+Na)^+$; HRMS (FAB) calcd for $C_{63}H_{120}NaO_{11}Si_3$ $[(M+Na)^+]$ 1159.8036, found 1159.8040.

3.1.32. Bisdimethylglycine ester 42. To a mixture of alcohol **41** (1.0 mg, 0.88 μmol), *N*,*N*-dimethylglycine (2.8 mg, 0.027 mmol), DMAP (8.2 mg, 0.067 mmol), and (±)-camphorsulfonic acid (7.2 mg, 0.031 mmol) was added a 0.188 M solution of DCC in CH_2Cl_2 (0.16 mL, 0.030 mmol) at room temperature. The mixture was stirred at room temperature for 16.5 h and diluted with saturated aqueous $NaHCO_3$ (1.5 mL). The mixture was stirred for 30 min and extracted with EtOAc (3×10 mL). The combined extracts were washed with brine (2 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (1 g, hexane–acetone 5:1→4:1→3:1) and preparative TLC on silica gel (200×100×0.25 mm^3, hexane–EtOAc–MeOH 10:5:1; 200×100×0.25 mm^3, benzene–EtOAc 1:1) to give **42** (0.9 mg, 80%) as a colorless oil: $[\alpha]_D^{29}=+6.3$ (*c* 0.23, MeOH); IR ($CHCl_3$) 1740, 1725, 1640, 1460, 1375, 1250, 1095, 970, 835 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.23 (dd, *J*=10.7, 15.1 Hz, 1H), 6.39 (dd, *J*=10.7, 15.1 Hz, 1H), 6.24 (ddd, *J*=5.9, 8.8, 15.1 Hz, 1H), 5.98 (d, *J*=15.1 Hz, 1H), 5.55 (ddd, *J*=4.4, 10.7, 15.1 Hz, 1H), 5.40 (ddd, *J*=7.2, 7.2, 15.1 Hz, 1H), 5.30 (ddd, *J*=2.0, 4.9, 10.7 Hz, 1H), 5.13 (dd, *J*=8.8, 15.1 Hz, 1H), 5.06 (dd, *J*=8.8, 15.1 Hz, 1H), 4.97 (br dd, *J*=5.9, 5.9 Hz, 1H), 4.83–4.78 (m, 2H), 3.73 (ddd, *J*=3.9, 6.3, 10.2 Hz, 1H), 3.66–3.60 (m, 2H), 3.55 (dd, *J*=4.9, 4.9 Hz, 1H), 3.52–3.45 (m, 2H), 3.19 (s, 2H), 3.18 (s, 3H), 3.12 (s, 3H), 3.10 (s, 2H), 2.59–2.28 (m, 6H), 2.32 (s, 6H), 2.30 (s, 6H), 1.98 (s, 3H), 1.90–1.06 (m, 19H), 0.98 (d, *J*=6.8 Hz, 3H), 0.98–0.90 (m, 12H), 0.94 (s, 9H), 0.90 (s, 9H), 0.90 (s, 9H), 0.87 (d, *J*=6.8 Hz, 3H), 0.77 (d, *J*=6.4 Hz, 3H), 0.16 (s, 3H), 0.11 (s, 3H), 0.07 (s, 6H), 0.06 (s, 6H); MS (FAB) *m/z* 1329 $(M+Na)^+$; HRMS (FAB) calcd for $C_{71}H_{134}N_2NaO_{13}Si_3$ $[(M+Na)^+]$ 1329.9091, found 1329.9110.

3.1.33. Analog 43. The experimental procedure was similar to that described for compound **32**. **43** (94% yield): a colorless amorphous powder; $[\alpha]_D^{29}=+64$ (*c* 0.028, MeOH); UV (MeCN) λ_{max} 262 nm (ε 31,000); IR ($CHCl_3$) 3480 (br), 1730, 1695, 1640, 1620, 1460, 1370, 1245, 1195, 1145, 1090, 970 cm^{-1}; ^1H NMR (600 MHz, acetone-d_6) δ 7.23 (dd, *J*=11.0, 15.0 Hz, 1H), 6.44 (dd, *J*=11.0, 15.0 Hz, 1H), 6.29 (ddd, *J*=5.1, 9.9, 15.0 Hz, 1H), 5.97 (d, *J*=15.0 Hz, 1H), 5.61 (ddd, *J*=4.0, 11.0, 15.0 Hz, 1H), 5.47 (br d, *J*=11.0 Hz, 1H), 5.38 (ddd, *J*=4.0, 11.0, 15.0 Hz, 1H), 5.10 (ddd, *J*=1.5, 9.2, 15.0 Hz, 1H), 5.02–4.97 (m, 2H), 4.78 (dd, *J*=2.6, 9.9 Hz, 1H), 4.72 (ddd, *J*=2.6, 3.7, 10.3 Hz, 1H), 3.65 (m, 1H), 3.58 (d, *J*=5.1 Hz, 1H), 3.55–3.46 (m, 5H), 3.30 (m, 1H), 3.21 (d, *J*=16.1 Hz, 1H), 3.18 (s, 3H), 3.17 (d, *J*=16.1 Hz, 1H), 3.10 (s, 3H), 3.09 (s, 2H), 3.06 (ddd, *J*=2.6, 5.1, 9.2 Hz, 1H), 2.48–2.41 (m, 2H), 2.31 (s, 6H), 2.30 (s, 6H), 2.30 (m, 1H), 2.15 (m, 1H), 2.08–1.12 (m, 21H), 1.97 (s, 3H), 0.99 (d, *J*=7.0 Hz, 3H), 0.99 (d, *J*=7.0 Hz, 3H), 0.98 (d, *J*=7.0 Hz, 3H), 0.96 (d, *J*=7.0 Hz, 3H), 0.90 (d, *J*=7.0 Hz, 3H), 0.87 (d, *J*=7.0 Hz, 3H), 0.71 (d, *J*=6.6 Hz, 3H); MS (FAB) *m/z* 987 $(M+Na)^+$; HRMS (FAB) calcd for $C_{59}H_{92}N_2NaO_{13}$ $[(M+Na)^+]$ 987.6497, found 987.6520.

3.1.34. Aldol 45. To a mixture of $Sn(OTf)_2$ (8.0 g, 18.4 mmol) and Et_3N (3.2 mL, 23 mmol) in CH_2Cl_2 (70 mL) was added a solution of ketone **44** (3.85 g, 14.1 mmol) in CH_2Cl_2 (4 mL) at −78°C, and the mixture was stirred at the same temperature for 2 h. A solution of 3-(benzyloxy)propanal (4.15 g, 25.3 mmol) in CH_2Cl_2 (6 mL) was added, and the reaction mixture was stirred at −78°C for 2 h, at −50°C for 2 h, and at −20°C for 12 h. The reaction mixture was diluted with 0.5 M phosphate buffer (pH 7.0, 200 mL), and the organic layer was separated. After the aqueous layer was extracted with Et_2O (3×150 mL), the organic layer and the ethereal extracts were combined, washed with 0.5 M phosphate buffer (pH 7.0, 80 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (160 g, hexane–acetone 25:1→20:1→18:1) and MPLC (Develosil Lop 60, 150 g, hexane–acetone 20:1→18:1, 10 mL/min) to give **45** (t_R=63 min, 5.08 g, 83%) as a colorless oil: $[\alpha]_D^{28}=+26.5$ (*c* 1.26, $CHCl_3$); IR ($CHCl_3$) 3500 (br), 1700, 1595, 1460, 1365, 1245, 1100, 1000, 880 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.27 (m, 5H), 4.51 (s, 2H), 4.21 (ddd, *J*=2.9, 6.4, 9.3 Hz, 1H), 3.87 (dd, *J*=9.3, 9.3 Hz, 1H), 3.68–3.60 (m, 3H), 3.27 (d, *J*=2.4 Hz, 1H, OH), 3.05 (m, 1H), 2.77 (ddq, *J*=4.2, 14.1, 6.8 Hz, 1H), 1.80 (m, 1H), 1.68 (m, 1H), 1.44 (d, *J*=6.8 Hz, 3H), 1.00

(d, J=7.2 Hz, 3H), 1.11–1.01 (m, 21H); MS (FAB) m/z 459 $(M+Na)^+$; HRMS (FAB) calcd for $C_{25}H_{44}NaO_4Si$ [$(M+Na)^+$] 459.2906, found 459.2905.

3.1.35. Diol 46. To a solution of $Me_4NBH(OAc)_3$ (3.13 g, 11.9 mmol) in CH_3CN (9.5 mL) and AcOH (9.5 mL) was added a solution of aldol **45** (1.12 g, 2.57 mmol) in CH_3CN (3 mL) at −40°C, and the mixture was stirred at −20°C for 25 h. Since the reaction was not completed, $Me_4NBH(OAc)_3$ (4.63 g, 17.6 mmol) was added by portions over 44 h and the mixture was further stirred at −20°C for 38 h. To the mixture was added 1 M aqueous potassium sodium tartrate (60 mL), and the mixture was stirred at room temperature for 1 h. The mixture was diluted with saturated aqueous $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (3×70 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (10 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (100 g, hexane–Et_2O 4:1→3:1→2:1 and 50 g, hexane–Et_2O 5:1→4:1) to give **46** (0.89 g, 80%) as a colorless oil: $[\alpha]_D^{31}$=−1.65 (c 1.39, $CHCl_3$); IR ($CHCl_3$) 3420 (br), 1595, 1460, 1360, 1080, 1015, 880 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.36–7.29 (m, 5H), 4.85 (d, J=1.7 Hz, 1H), 4.52 (s, 2H), 4.18 (m, 1H), 4.02 (d, J=1.3 Hz, 1H), 3.89 (dd, J=4.1, 9.9 Hz, 1H), 3.70 (dd, J=8.1, 9.9 Hz, 1H), 3.65 (dd, J=6.4, 6.4 Hz, 2H), 3.60 (m, 1H), 2.04 (m, 1H), 1.91 (m, 1H), 1.74 (m, 1H), 1.63 (m, 1H), 1.11–1.03 (m, 24H), 0.81 (d, J=6.9 Hz, 3H); MS (FAB) m/z 461 $(M+Na)^+$; HRMS (FAB) calcd for $C_{25}H_{46}NaO_4Si$ [$(M+Na)^+$] 461.3063, found 461.3061.

3.1.36. Triol 47. A mixture of diol **46** (0.87 g, 2.0 mmol) and 20% $Pd(OH)_2$/C (0.20 g) in 1,4-dioxane (5 mL) was stirred under hydrogen at room temperature for 15 min. The mixture was filtered through a pad of Celite, and the residue was washed with EtOAc (200 mL). The filtrate and washings were combined and concentrated. The residue was purified by column chromatography on silica gel (25 g, hexane–Et_2O 5:1→3:1→1:1) to give **47** (0.69 g, 100%) as a colorless oil: $[\alpha]_D^{30}$=+9.82 (c 1.07, $CHCl_3$); IR ($CHCl_3$) 3410 (br), 1460, 1080, 1055, 1010, 880 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 5.01 (m, 1H), 4.33 (br s, 1H),4.23 (m, 1H), 3.95 (dd, J=3.6, 9.9 Hz, 1H), 3.84 (m, 2H), 3.69 (dd, J=8.6, 9.9 Hz, 1H), 3.63 (ddd, J=2.0, 3.6, 7.9 Hz, 1H), 2.92 (dd, J=3.3, 6.9 Hz, 1H), 2.06 (m, 1H), 1.92 (m, 1H), 1.70 (m, 1H), 1.45 (m, 1H), 1.18–1.04 (m, 24H), 0.82 (d, J=6.9 Hz, 3H); MS (FAB) m/z 371 $(M+Na)^+$; HRMS (FAB) calcd for $C_{18}H_{40}NaO_4Si$ [$(M+Na)^+$] 371.2594, found 371.2599.

3.1.37. Sulfide 48. A solution of triol **47** (0.78 g, 2.2 mmol), PhSSPh (0.80 g, 3.7 mmol), and PBu_3 (0.80 mL, 3.2 mmol) in DMF (3.5 mL) was stirred at room temperature for 1.5 h. The mixture was diluted with H_2O (1 mL), stirred for 10 min, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (40 g, hexane–Et_2O 20:1→10:1→5:1) to give **48** (0.95 g, 93%) as a colorless oil: $[\alpha]_D^{31}$=−16.3 (c 1.36, $CHCl_3$); IR ($CHCl_3$) 3400 (br), 1585, 1460, 1080, 1055, 1015, 880 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.37–7.32 (m, 2H), 7.30–7.23 (m, 2H), 7.15 (m, 1H), 5.00 (m, 1H), 4.14 (m, 1H), 4.10 (br s, 1H), 3.95 (dd, J=3.6, 9.9 Hz, 1H), 3.68 (dd, J=8.6, 9.9 Hz, 1H), 3.62 (ddd, J=2.0, 3.6, 7.9 Hz, 1H), 3.15 (ddd, J=5.4, 8.4, 13.2 Hz, 1H), 3.00 (ddd, J=7.1, 8.1, 13.2 Hz, 1H), 2.03 (m, 1H), 1.96 (m, 1H), 1.70 (m, 1H), 1.59 (m, 1H), 1.19–1.04 (m, 21H), 1.02 (d, J=7.3 Hz, 3H), 0.81 (d, J=6.9 Hz, 3H); MS (FAB) m/z 463 $(M+Na)^+$; HRMS (FAB) calcd for $C_{24}H_{44}NaO_3SSi$ [$(M+Na)^+$] 463.2678, found 463.2657.

3.1.38. Triol 49. To a solution of sulfide **48** (0.87 g, 2.0 mmol) in THF (4 mL) was added a 1 M solution of Bu_4NF in THF (4 mL, 4 mmol), and the mixture was stirred at room temperature for 3 h. The mixture was diluted with saturated aqueous NH_4Cl (10 mL) and extracted with Et_2O (3×10 mL). The combined extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (25 g, hexane–Et_2O 4:1→2:1→1:2) to give **49** (0.69 g, 100%) as a colorless oil: $[\alpha]_D^{29}$=−16.0 (c 1.09, $CHCl_3$); IR ($CHCl_3$) 3400 (br), 1580, 1460, 1090, 1050, 970 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.38–7.27 (m, 4H), 7.19 (m, 1H), 4.69 (br s, 1H), 4.22 (m, 1H), 3.95 (br s, 1H), 3.86 (dd, J=3.3, 10.6 Hz, 1H), 3.68–3.58 (m, 2H), 3.51 (br s, 1H), 3.12 (ddd, J=5.7, 9.9, 13.0 Hz, 1H), 3.01 (td, J=7.3, 13.0 Hz, 1H), 2.08–1.59 (m, 4H), 1.02 (d, J=7.3 Hz, 3H), 0.86 (d, J=6.9 Hz, 3H); MS (FAB) m/z 307 $(M+Na)^+$; HRMS (FAB) calcd for $C_{15}H_{24}NaO_3S$ [$(M+Na)^+$] 307.1344, found 307.1324.

3.1.39. Trityl ether 50. A solution of triol **49** (0.52 g, 1.8 mmol) and trityl chloride (0.88 g, 3.2 mmol) in pyridine (4 mL) was stirred at 50°C for 11.5 h. After ice (2 g) was added to the reaction mixture, the mixture was stirred for 10 min, diluted with H_2O (10 mL), and extracted with Et_2O (3×50 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2×30 mL) and brine (30 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (25 g, hexane–Et_2O–Et_3N 5:1:0.06→2:1:0→1:2:0) to give **50** (0.92 g, 96%) as a colorless oil: $[\alpha]_D^{30}$=+9.88 (c 1.00, $CHCl_3$); IR ($CHCl_3$) 3440 (br), 1595, 1580, 1450, 1090, 1050, 975, 900 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.43–7.13 (m, 20H), 4.38 (d, J=2.0 Hz, 1H), 4.11 (m, 1H), 3.83 (d, J=1.3 Hz, 1H), 3.46 (m, 1H), 3.39 (dd, J=3.6, 10.6 Hz, 1H), 3.14 (ddd, J=5.8, 8.6, 13.9 Hz, 1H), 3.10 (dd, J=8.1, 10.6 Hz, 1H), 2.99 (ddd, J=7.6, 7.6, 13.9 Hz, 1H), 2.13–2.03 (m, 2H), 2.00–1.86 (m, 2H), 0.94 (d, J=7.3 Hz, 3H), 0.80 (d, J=6.9 Hz, 3H); MS (FAB) m/z 549 $(M+Na)^+$; HRMS (FAB) calcd for $C_{34}H_{38}NaO_3S$ [$(M+Na)^+$] 549.2439, found 549.2429.

3.1.40. Silyl ether 51. To a solution of trityl ether **50** (0.92 g, 1.7 mmol) in DMF (4 mL) were added imidazole (0.68 g, 10 mmol) and Et_3SiCl (0.84 mL, 5.0 mmol). After the mixture was stirred at 50°C for 1.5 h, H_2O (2 mL) was added. The mixture was stirred for 10 min, diluted with H_2O (10 mL), and extracted with Et_2O (3×40 mL). The combined extracts were washed with brine (30 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (30 g, hexane–Et_2O 40:1) to give **51** (1.22 g, 93%) as a colorless oil: $[\alpha]_D^{29}$=−16.2 (c 1.01, $CHCl_3$); IR ($CHCl_3$) 1595, 1580, 1450, 1065, 1010, 910 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.47–7.14 (m, 20H), 3.84 (ddd, J=5.6, 5.6, 5.6 Hz, 1H), 3.55 (dd, J=2.6, 6.6 Hz, 1H), 3.24 (dd, J=4.8, 9.1 Hz, 1H), 2.84–2.77 (m, 3H), 2.08 (m, 1H), 1.82–1.73 (m, 2H), 1.60 (m,

1H), 1.02 (d, *J*=6.9 Hz, 3H), 0.94 (t, *J*=7.6 Hz, 9H), 0.85 (t, *J*=7.6 Hz, 9H), 0.70 (d, *J*=6.9 Hz, 3H), 0.57 (q, *J*=7.6 Hz, 6H), 0.49 (q, *J*=6.9 Hz, 6H); MS (FAB) *m/z* 777 $(M+Na)^+$; HRMS (FAB) calcd for $C_{46}H_{66}NaO_3SSi_2$ $[(M+Na)^+]$ 777.4169, found 777.4174.

3.1.41. Sulfone 52. To a solution of silyl ether **51** (1.18 g, 1.56 mmol) in CH_2Cl_2 (10 mL) were added $NaHCO_3$ (0.88 g, 10.4 mmol) and *m*-chloroperbenzoic acid (0.83 g, 4.8 mmol). After the mixture was stirred at room temperature for 1.5 h, saturated aqueous $Na_2S_2O_3$ (2 mL) and H_2O (10 mL) were added. The mixture was stirred for 1 h and extracted with Et_2O (3×20 mL). The combined extracts were successively washed with saturated aqueous $NaHCO_3$ (10 mL), H_2O (10 mL), and brine (10 mL), and then dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography on silica gel (40 g, hexane–Et_2O 20:1→10:1) to give **52** (1.20 g, 98%) as a colorless oil: $[\alpha]_D^{29}=-5.73$ (*c* 1.18, $CHCl_3$); IR ($CHCl_3$) 1595, 1585, 1450, 1305, 1150, 1060, 1010, 910 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.87–7.83 (m, 2H), 7.61 (m, 1H), 7.55–7.50 (m, 2H), 7.43–7.36 (m, 6H), 7.30–7.21 (m, 9H), 3.71 (ddd, *J*=5.6, 5.6, 5.6 Hz, 1H), 3.45 (dd, *J*=3.0, 6.3 Hz, 1H), 3.15 (dd, *J*=5.1, 9.0 Hz, 1H), 3.10–2.89 (m, 2H), 2.79 (dd, *J*=9.0, 9.0 Hz, 1H), 1.95 (m, 1H), 1.89–1.72 (m, 2H), 1.41 (ddd, *J*=6.9, 6.9, 6.9 Hz, 1H), 0.94 (d, *J*=6.9 Hz, 3H), 0.88 (t, *J*=7.6 Hz, 9H), 0.81 (t, *J*=7.6 Hz, 9H), 0.66 (d, *J*=6.9 Hz, 3H), 0.50 (q, *J*=7.6 Hz, 6H), 0.43 (q, *J*=6.9 Hz, 6H); MS (FAB) *m/z* 809 $(M+Na)^+$; HRMS (FAB) calcd for $C_{46}H_{66}NaO_5SSi_2$ $[(M+Na)^+]$ 809.4066, found 809.4057.

3.1.42. Olefin 53. The experimental procedure was similar to that described for compound **17**. **53** (73% yield, 20*E*/20*Z*=10:1): a colorless oil; $[\alpha]_D^{30}=+20.3$ (*c* 1.02, $CHCl_3$); IR ($CHCl_3$) 1720, 1600, 1460, 1160, 1090, 1020, 970, 835 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) (20*E*-isomer) δ 7.44–7.42 (m, 6H), 7.29–7.25 (m, 6H), 7.22–7.19 (m, 3H), 5.54 (ddd, *J*=7.3, 7.3, 15.4 Hz, 1H), 5.47 (ddd, *J*=7.3, 7.3, 15.4 Hz, 1H), 5.22 (dd, *J*=7.8, 15.4 Hz, 1H), 5.19 (dd, *J*=8.3, 15.4 Hz, 1H) 4.64 (d, *J*=11.5 Hz, 1H), 4.58 (d, *J*=11.5 Hz, 1H), 4.21–4.10 (m, 2H), 3.87 (m, 1H), 3.65–3.57 (m, 2H) 3.52 (dd, *J*=3.4, 3.4 Hz, 1H), 3.47 (ddd, *J*=7.3, 7.3, 7.3 Hz, 1H), 3.41 (ddd, *J*=7.3, 7.3, 7.3 Hz, 1H), 3.23 (s, 3H), 3.20 (m, 1H), 3.09 (s, 3H), 2.83 (dd, *J*=9.0, 9.0 Hz, 1H), 2.28–2.24 (m, 2H), 2.16 (s, 3H), 2.16–2.08 (m, 2H), 1.97 (m, 1H), 1.88–1.78 (m, 2H), 1.72 (m, 1H), 1.67–1.34 (m, 8H), 1.21 (s, 9H), 1.09 (m, 1H), 1.04 (d, *J*=6.8 Hz, 3H), 0.96 (t, *J*=7.8 Hz, 9H), 0.91–0.86 (m, 6H), 0.90 (s, 9H), 0.85 (d, *J*=6.8 Hz, 3H), 0.85 (t, *J*=7.8 Hz, 9H), 0.66 (d, *J*=6.8 Hz, 3H), 0.59 (q, *J*=7.8 Hz, 6H), 0.50 (q, *J*=7.8 Hz, 6H), 0.06 (s, 3H), 0.06 (s, 3H); MS (FAB) *m/z* 1297 $(M+Na)^+$; HRMS (FAB) calcd for $C_{74}H_{126}NaO_9SSi_3$ $[(M+Na)^+]$ 1297.8328, found 1297.8340.

3.1.43. Alcohol 54. The experimental procedure was similar to that described for compound **18**. **54** (96% yield, 20*E*/20*Z*=10:1): a colorless oil; $[\alpha]_D^{31}=+27.7$ (*c* 1.16, $CHCl_3$); IR ($CHCl_3$) 3500 (br), 1600, 1460, 1380, 1255, 1090, 1035, 975, 835 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) (20*E*-isomer) δ 7.44–7.42 (m, 6H), 7.29–7.25 (m, 6H), 7.22–7.19 (m, 3H), 5.54 (ddd, *J*=7.3, 7.3, 15.4 Hz, 1H), 5.46 (ddd, *J*=7.3, 7.3, 15.4 Hz, 1H), 5.23 (dd, *J*=8.3, 15.4 Hz, 1H), 5.18 (dd, *J*=8.3, 15.4 Hz, 1H), 4.69 (d, *J*=11.7 Hz, 1H), 4.59 (d, *J*=11.7 Hz, 1H), 3.86 (m, 1H), 3.81–3.68 (m, 3H), 3.60 (dd, *J*=2.4, 7.3 Hz, 1H), 3.50 (dd, *J*=2.9, 4.4 Hz, 1H), 3.48–3.39 (m, 2H), 3.23 (s, 3H) 3.20 (m, 1H), 3.09 (s, 3H), 2.82 (dd, *J*=8.8, 8.8 Hz, 1H), 2.51 (br s, 1H), 2.28–2.23 (m, 2H), 2.21 (s, 3H), 2.16–2.06 (m, 2H), 1.99 (m, 1H), 1.84 (m, 1H), 1.74–1.33 (m, 10H), 1.11 (m, 1H), 1.03 (d, *J*=6.8 Hz, 3H), 0.95 (t, *J*=7.8 Hz, 9H), 0.91–0.86 (m, 6H), 0.90 (s, 9H), 0.85 (d, *J*=6.8 Hz, 3H), 0.85 (t, *J*=7.8 Hz, 9H), 0.65 (d, *J*=6.8 Hz, 3H), 0.59 (q, *J*=7.8 Hz, 6H), 0.50 (q, *J*=7.8 Hz, 6H), 0.05 (s, 3H), 0.05 (s, 3H); MS (FAB) *m/z* 1191 $(M+H)^+$; HRMS (FAB) calcd for $C_{69}H_{118}NaO_8SSi_3$ $[(M+Na)^+]$ 1213.7752, found 1213.7740.

3.1.44. Aldehyde 55. The experimental procedure was similar to that described for compound **19**. **55** (83% yield, 20*E*/20*Z*=10:1): a colorless oil; $[\alpha]_D^{28}=+9.61$ (*c* 0.915, $CHCl_3$); IR ($CHCl_3$) 2730, 1725, 1595, 1515, 1460, 1380, 1240, 1110, 1040, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (20*E*-isomer) δ 9.82 (dd, *J*=2.0, 2.9 Hz, 1H), 7.44–7.42 (m, 6H), 7.29–7.18 (m, 9H), 5.54 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.46 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.22 (dd, *J*=8.3, 15.1 Hz, 1H), 5.18 (dd, *J*=8.3, 15.1 Hz, 1H), 4.66 (d, *J*=11.7 Hz, 1H), 4.60 (d, *J*=11.7 Hz, 1H), 4.06 (m, 1H), 3.86 (m, 1H), 3.60 (dd, *J*=3.4, 8.0 Hz, 1H), 3.57 (dd, *J*=3.4, 3.4 Hz, 1H), 3.23 (s, 3H), 3.47 (ddd, *J*=6.8, 6.8, 6.8 Hz, 1H), 3.41 (ddd, *J*=6.8, 6.8, 6.8 Hz, 1H), 3.20 (m, 1H), 3.09 (s, 3H), 2.82 (dd, *J*=9.0, 9.0 Hz, 1H), 2.60 (ddd, *J*=2.9, 7.8, 16.6 Hz, 1H), 2.53 (ddd, *J*=2.0, 3.9, 16.6 Hz, 1H), 2.33–2.21 (m, 2H), 2.13 (s, 3H), 2.10 (m, 1H), 2.00 (m, 1H), 1.84 (ddd, *J*=7.1, 7.3, 13.7 Hz, 1H), 1.66–1.33 (m, 9H), 1.10 (m, 1H), 1.03 (d, *J*=6.8 Hz, 3H), 0.95 (t, *J*=7.8 Hz, 9H), 0.90 (s, 9H), 0.90 (d, *J*=6.8 Hz, 3H), 0.88 (d, *J*=7.3 Hz, 3H), 0.85 (t, *J*=7.8 Hz, 9H), 0.85 (d, *J*=6.8 Hz, 3H), 0.66 (d, *J*=7.3 Hz, 3H), 0.59 (q, *J*=7.8 Hz, 6H), 0.50 (q, *J*=7.8 Hz, 6H), 0.05 (s, 6H); MS (FAB) *m/z* 1211 $(M+Na)^+$; HRMS (FAB) calcd for $C_{69}H_{116}NaO_8SSi_3$ $[(M+Na)^+]$ 1211.7597, found 1211.7570.

3.1.45. α,β,γ,δ-Unsaturated ester 56. The experimental procedure was similar to that described for compound **20**. **56** (94% yield, 4*E*/4*Z*=30:1, 20*E*/20*Z*=10:1): a colorless oil; $[\alpha]_D^{28}=-5.71$ (*c* 0.947, $CHCl_3$); IR ($CHCl_3$) 1700, 1640, 1615, 1595, 1460, 1370, 1250, 1090, 1045, 975, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (4*E*,20*E*-isomer) δ 7.44–7.42 (m, 6H), 7.29–7.18 (m, 10H), 6.25 (dd, *J*=10.2, 15.1 Hz, 1H), 6.17 (ddd, *J*=6.8, 6.8, 15.1 Hz, 1H), 5.80 (d, *J*=15.1 Hz, 1H), 5.54 (ddd, *J*=7.3, 7.3, 15.6 Hz, 1H), 5.46 (ddd, *J*=7.8, 7.8, 15.6 Hz, 1H), 5.22 (dd, *J*=8.3, 15.6 Hz, 1H), 5.18 (dd, *J*=8.3, 15.6 Hz, 1H), 4.62 (d, *J*=11.7 Hz, 1H), 4.58 (d, *J*=11.7 Hz, 1H), 4.19 (q, *J*=7.1 Hz, 2H), 3.86 (m, 1H), 3.63 (dd, *J*=3.4, 3.4 Hz, 1H), 3.62–3.54 (m, 2H), 3.48 (ddd, *J*=7.1, 7.1, 7.1 Hz, 1H), 3.41 (ddd, *J*=6.1, 6.1, 6.1 Hz, 1H), 3.23 (s, 3H), 3.20 (m, 1H), 3.09 (s, 3H), 2.82 (dd, *J*=9.0, 9.0 Hz, 1H), 2.45 (m, 1H), 2.34–2.26 (m, 3H), 2.14 (s, 3H), 2.12–2.08 (m, 2H), 1.89–1.80 (m, 2H), 1.63–1.33 (m, 8H), 1.29 (t, *J*=7.1 Hz, 3H), 1.08 (m, 1H), 1.03 (d, *J*=6.8 Hz, 3H), 0.95 (t, *J*=7.8 Hz, 9H), 0.90 (s, 9H), 0.87 (m, 3H), 0.85 (t, *J*=7.8 Hz, 9H), 0.85 (d, *J*=6.8 Hz, 3H), 0.85 (d, *J*=6.8 Hz, 3H), 0.65 (d, *J*=6.8 Hz, 3H), 0.59 (q, *J*=7.8 Hz, 6H), 0.50 (q, *J*=7.8 Hz, 6H), 0.06 (s, 3H) 0.05 (s, 3H); MS (FAB) *m/z* 1307 $(M+Na)^+$; HRMS

(FAB) calcd for $C_{75}H_{124}NaO_9SSi_3$ [$(M+Na)^+$] 1307.8171, found 1307.8170.

3.1.46. Diol 57. The experimental procedure was similar to that described for compound **21**. **57** (91% yield, 4*E*/4*Z*=30:1, 20*E*/20*Z*=10:1): a colorless oil; $[\alpha]_D^{28}$=+8.90 (*c* 0.963, $CHCl_3$); IR ($CHCl_3$) 3450 (br), 1705, 1645, 1615, 1590, 1460, 1375, 1250, 1100, 1045, 975, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (4*E*,20*E*-isomer) δ 7.44–7.42 (m, 6H), 7.34–7.23 (m, 10H), 6.25 (dd, *J*=10.2, 15.1 Hz, 1H), 6.18 (ddd, *J*=6.3, 6.3, 15.1 Hz, 1H), 5.80 (d, *J*=15.1 Hz, 1H), 5.63 (ddd, *J*=7.8, 7.8, 15.1 Hz, 1H), 5.54 (ddd, *J*=7.5, 7.5, 15.1 Hz, 1H), 5.31 (dd, *J*=8.3, 15.1 Hz, 1H), 5.23 (dd, *J*=8.3, 15.1 Hz, 1H), 4.62 (d, *J*=11.5 Hz, 1H), 4.58 (d, *J*=11.5 Hz, 1H), 4.39 (br s, 1H), 4.19 (q, *J*=7.1 Hz, 2H), 4.01 (m, 1H), 3.83 (br s, 1H), 3.63 (dd, *J*=3.4, 3.4 Hz, 1H), 3.59–3.53 (m, 2H), 3.49 (m, 1H), 3.42 (m, 1H), 3.39 (dd, *J*=3.9, 8.8 Hz, 1H), 3.23 (s, 3H), 3.22 (s, 3H), 3.11 (dd, *J*=8.8, 8.8 Hz, 1H), 2.45 (m, 1H), 2.37–2.27 (m, 2H), 2.17–2.08 (m, 2H), 2.14 (s, 3H), 1.92–1.82 (m, 2H), 1.64–1.39 (m, 10H), 1.29 (t, *J*=7.1 Hz, 3H), 1.01 (d, *J*=7.3 Hz, 3H), 0.90 (s, 9H), 0.88 (m, 3H), 0.87 (d, *J*=6.3 Hz, 3H), 0.85 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.8 Hz, 3H), 0.06 (s, 3H) 0.05 (s, 3H); MS (FAB) *m*/*z* 1079 $(M+Na)^+$; HRMS (FAB) calcd for $C_{63}H_{96}NaO_9SSi$ [$(M+Na)^+$] 1079.6442, found 1079.6430.

3.1.47. 24-Membered lactone 59 and a 26-membered lactone. The experimental procedure was similar to that described for compound **23** and a 26-membered lactone. **59** (49% yield from **57**): a colorless oil; $[\alpha]_D^{30}$=+39.7 (*c* 1.13, $CHCl_3$); IR ($CHCl_3$) 3500 (br), 1690, 1640, 1615, 1590, 1460, 1380, 1260, 1075, 1050, 975, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44–7.42 (m, 6H), 7.31–7.20 (m, 10H), 6.26–6.15 (m, 2H), 5.80 (d, *J*=15.1 Hz, 1H), 5.55 (ddd, *J*=4.4, 10.4, 15.2 Hz, 1H), 5.40 (br d, *J*=11.2 Hz, 1H), 5.28 (ddd, *J*=6.3, 8.3, 15.2 Hz, 1H), 5.10 (dd, *J*=8.8, 15.2 Hz, 1H), 5.10 (dd, *J*=8.8, 15.2 Hz, 1H), 4.60 (d, *J*=11.2 Hz, 1H), 4.58 (d, *J*=11.2 Hz, 1H), 3.62–3.45 (m, 3H), 3.41 (ddd, *J*=3.9, 9.3, 9.3 Hz, 1H), 3.06 (ddd, *J*=3.9, 6.8, 10.2 Hz, 1H), 3.29–3.23 (m, 2H), 3.24 (s, 3H), 3.20 (s, 3H), 3.11 (dd, *J*=5.4, 9.3 Hz, 1H), 2.44–2.31 (m, 2H), 2.24 (m, 1H), 2.17 (s, 3H), 2.10 (m, 1H), 2.00 (m, 1H), 1.98–1.80 (m, 3H), 1.62–1.11 (m, 9H), 1.13 (d, *J*=6.8 Hz, 3H), 0.92 (d, *J*=6.8 Hz, 3H), 0.89 (s, 9H), 0.88 (m, 3H), 0.80 (d, *J*=6.8 Hz, 3H), 0.74 (d, *J*=5.9 Hz, 3H), 0.05 (s, 3H), 0.04 (s, 3H); MS (FAB) *m*/*z* 1033 $(M+Na)^+$; HRMS (FAB) calcd for $C_{61}H_{90}NaO_8SSi$ [$(M+Na)^+$] 1033.6022, found 1033.6030.

26-Membered lactone (19% yield from **57**): a colorless oil; $[\alpha]_D^{29}$=+19.0 (*c* 0.977, $CHCl_3$); IR ($CHCl_3$) 3500 (br), 1685, 1640, 1615, 1590, 1460, 1360, 1255, 1090, 1005, 975, 835 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.46–7.44 (m, 6H), 7.32–7.23 (m, 9H), 7.06 (dd, *J*=10.7, 15.1 Hz, 1H), 6.25 (dd, *J*=10.7, 15.1 Hz, 1H), 6.13 (ddd, *J*=6.8, 7.2, 15.1 Hz, 1H), 5.71 (d, *J*=15.1 Hz, 1H), 5.47–5.38 (m, 2H), 5.23 (dd, *J*=8.3, 15.1 Hz, 1H), 5.19 (dd, *J*=8.3, 15.1 Hz, 1H), 4.87 (dd, *J*=2.4, 10.7 Hz, 1H), 4.65 (d, *J*=11.5 Hz, 1H), 4.61 (d, *J*=11.5 Hz, 1H), 3.73 (m, 1H), 3.60 (m, 1H), 3.46–3.38 (m, 2H), 3.34 (m, 1H), 3.28 (dd, *J*=5.6, 9.0 Hz, 1H), 3.22 (s, 3H), 3.17 (s, 3H), 3.03 (dd, *J*=8.3, 9.0 Hz, 1H), 2.75 (d, *J*=3.9 Hz, 1H), 2.49–2.23 (m, 4H), 2.17 (s, 3H), 2.08 (m, 1H), 2.00–1.88 (m, 2H) 1.84 (m, 1H), 1.75 (m, 1H), 1.66–1.08 (m, 8H), 0.98 (d, *J*=6.8 Hz, 3H), 0.93 (d, *J*=6.8 Hz, 3H), 0.90 (s, 9H), 0.88 (m, 3H), 0.87 (d, *J*=7.3 Hz, 3H), 0.72 (d, *J*=6.8 Hz, 3H), 0.06 (s, 3H) 0.05 (s, 3H); MS (FAB) *m*/*z* 1033 $(M+Na)^+$; HRMS (FAB) calcd for $C_{61}H_{90}NaO_8SSi$ [$(M+Na)^+$] 1033.6022, found 1033.6040.

3.1.48. Isomerization of a 26-membered lactone to the 26-membered lactone 59. The experimental procedure was similar to that described for isomerization of a 26-membered lactone to **23** (78% yield).

3.1.49. Silyl ether 60. The experimental procedure was similar to that described for compound **24**. **60** (86% yield): a colorless oil; $[\alpha]_D^{29}$=+13.5 (*c* 1.00, $CHCl_3$); IR ($CHCl_3$) 1705, 1640, 1615, 1595, 1515, 1460, 1360, 1255, 1075, 1045, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43–7.41 (m, 6H), 7.29–7.19 (m, 10H), 6.22–6.18 (m, 2H), 5.79 (d, *J*=15.6 Hz, 1H), 5.52 (ddd, *J*=4.1, 10.5, 15.1 Hz, 1H), 5.28 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.22 (m, 1H), 5.12 (dd, *J*=8.8, 15.1 Hz, 1H), 5.09 (dd, *J*=8.8, 15.1 Hz, 1H), 4.60 (d, *J*=11.7 Hz, 1H), 4.55 (d, *J*=11.7 Hz, 1H), 3.60–3.54 (m, 3H), 3.49 (ddd, *J*=4.9, 9.0, 9.0 Hz, 1H), 3.41 (ddd, *J*=3.7, 9.0, 9.0 Hz, 1H), 3.25 (m, 1H), 3.24 (s, 3H), 3.20 (s, 3H), 2.79 (dd, *J*=9.0, 9.0 Hz, 1H), 2.43–2.07 (m, 5H), 2.17 (s, 3H), 1.90–1.80 (m, 3H), 1.69–1.12 (m, 9H), 1.03 (d, *J*=6.8 Hz, 3H), 0.93 (d, *J*=6.8 Hz, 3H), 0.89 (s, 9H), 0.87 (d, *J*=6.8 Hz, 3H), 0.83 (d, *J*=7.3 Hz, 3H), 0.77 (d, *J*=6.3 Hz, 3H), 0.74 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H), 0.04 (s, 3H), −0.11 (s, 3H); MS (FAB) *m*/*z* 1147 $(M+Na)^+$; HRMS (FAB) calcd for $C_{67}H_{104}NaO_8SSi_2$ [$(M+Na)^+$] 1147.6889, found 1147.6880.

3.1.50. Alcohol 61. The experimental procedure was similar to that described for compound **30**. **61** (86% yield): a colorless oil; $[\alpha]_D^{28}$=+21.3 (*c* 1.05, $CHCl_3$); IR ($CHCl_3$) 3460 (br), 1705, 1640, 1615, 1595, 1460, 1360, 1265, 1090, 1070, 1035, 970, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43–7.41 (m, 6H), 7.29–7.19 (m, 10H), 6.27 (ddd, *J*=5.7, 8.1, 15.1 Hz, 1H), 6.21 (dd, *J*=10.0, 15.1 Hz, 1H), 5.77 (d, *J*=15.1 Hz, 1H), 5.49 (ddd, *J*=4.4, 10.3, 15.2 Hz, 1H), 5.40 (ddd, *J*=7.3, 7.3, 15.2 Hz, 1H), 5.22 (dd, *J*=8.8, 15.2 Hz, 1H), 5.22 (m, 1H), 5.14 (dd, *J*=8.8, 15.2 Hz, 1H), 3.78 (dd, *J*=2.9, 2.9 Hz, 1H), 3.59 (ddd, *J*=3.4, 5.9, 11.7 Hz, 1H), 3.55 (dd, *J*=4.4, 4.4 Hz, 1H), 3.52–3.46 (m, 2H), 3.25 (dd, *J*=5.1, 9.0 Hz, 1H), 3.23 (s, 3H), 3.20 (s, 3H), 3.09 (br s, 1H), 2.78 (dd, *J*=9.0, 9.0 Hz, 1H), 2.40 (m, 1H), 2.36–2.27 (m, 2H), 2.17 (ddd, *J*=10.5, 10.5, 14.1 Hz, 1H), 2.11 (m, 1H), 2.00 (ddd, *J*=6.8, 6.8, 13.2 Hz, 1H), 1.78 (ddd, *J*=6.3, 6.3, 13.2 Hz, 1H), 1.73–1.59 (m, 4H), 1.54–1.14 (m, 6H), 1.03 (d, *J*=6.8 Hz, 3H), 0.95 (d, *J*=6.8 Hz, 3H), 0.91 (s, 9H), 0.86 (d, *J*=6.8 Hz, 3H), 0.82 (d, *J*=7.3 Hz, 3H), 0.77 (d, *J*=6.3 Hz, 3H), 0.74 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H), 0.03 (s, 3H), −0.11 (s, 3H); MS (FAB) *m*/*z* 1087 $(M+Na)^+$; HRMS (FAB) calcd for $C_{65}H_{100}NaO_8Si_2$ [$(M+Na)^+$] 1087.6854, found 1087.6860.

3.1.51. Trimethylserine ester 62. The experimental procedure was similar to that described for compound **31**. **62** (93% yield, *S*/*R*=1:1): a colorless oil; $[\alpha]_D^{28}$=+49 (*c* 0.40, MeOH); IR ($CHCl_3$) 1710, 1645, 1620, 1600, 1450, 1360, 1245, 1085, 975 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6) δ

7.47–7.44 (m, 6H), 7.34–7.17 (m, 10H), 6.42 [6.45] (dd, *J*=10.7, 15.1 Hz, 1H), 6.29 [6.27] (ddd, *J*=4.9, 10.7, 15.1 Hz, 1H), 5.95 [5.95] (d, *J*=15.1 Hz, 1H), 5.57 (ddd, *J*=4.4, 10.7, 15.1 Hz, 1H), 5.42–5.33 (m, 2H), 5.10 (m, 1H), 4.97 (dd, *J*=9.3, 15.1 Hz, 1H), 4.76 (m, 1H), 3.68 (m, 1H), 3.58 [3.58] (dd, *J*=5.4, 9.3 Hz, 1H), 3.53–3.28 (m, 8H), 3.30 [3.32] (s, 3H), 3.18 (s, 3H), 3.10 (s, 3H), 3.03 (dd, *J*=6.8, 9.3 Hz, 1H), 2.50–1.85 (m, 10H), 2.36 [2.35] (s, 6H), 1.76–1.28 (m, 7H), 1.07 (d, *J*=6.8 Hz, 3H), 1.02–0.99 (m, 6H), 0.87 (d, *J*=6.8 Hz, 3H), 0.72 [0.71] (d, *J*=6.1 Hz, 3H). The counterparts of doubled signals in the ratio of 1:1 are in brackets; MS (FAB) *m/z* 1216 $(M+Na)^+$; HRMS (FAB) calcd for $C_{71}H_{111}NNaO_{10}Si_2$ $[(M+Na)^+]$ 1216.7645, found 1216.7680.

3.1.52. Diol 63 and triol 64. A solution of trimethylserine ester **62** (11.8 mg, 9.89 μmol) in a 8:3:5 mixture of THF, pyridine, and HF·pyridine (1 mL) was stirred at room temperature for 20 h and at 40°C for 19 h and poured into ice-cooled saturated aqueous $NaHCO_3$ (8 mL). The aqueous mixture was extracted with EtOAc (3×10 mL). The extracts were combined, washed with brine (5 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (3 g, hexane–acetone 1:1→1:2→1:3→1:4) to give **63** (5.0 mg, 52%, *S*/*R*=1:1) and **64** (3.1 mg, 43%, *S*/*R*=1:1) as a colorless oil, respectively. **63**: $[\alpha]_D^{28}$=+49 (*c* 0.40, MeOH); IR ($CHCl_3$) 1710, 1645, 1620, 1600, 1450, 1360, 1245, 1085, 975 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6) δ 7.47–7.44 (m, 6H), 7.34–7.17 (m, 10H), 6.42 [6.45] (dd, *J*=10.7, 15.1 Hz, 1H), 6.29 [6.27] (ddd, *J*=4.9, 10.7, 15.1 Hz, 1H), 5.95 [5.95] (d, *J*=15.1 Hz, 1H), 5.57 (ddd, *J*=4.4, 10.7, 15.1 Hz, 1H), 5.42–5.33 (m, 2H), 5.10 (m, 1H), 4.97 (dd, *J*=9.3, 15.1 Hz, 1H), 4.76 (m, 1H), 3.68 (m, 1H), 3.58 [3.58] (dd, *J*=5.4, 9.3 Hz, 1H), 3.53–3.28 (m, 8H), 3.30 [3.32] (s, 3H), 3.18 (s, 3H), 3.10 (s, 3H), 3.03 (dd, *J*=6.8, 9.3 Hz, 1H), 2.50–1.85 (m, 10H), 2.36 [2.35] (s, 6H), 1.76–1.28 (m, 7H), 1.07 (d, *J*=6.8 Hz, 3H), 1.02–0.99 (m, 6H), 0.87 (d, *J*=6.8 Hz, 3H), 0.72 [0.71] (d, *J*=6.1 Hz, 3H). The counterparts of doubled signals in the ratio of 1:1 are in brackets; MS (FAB) *m/z* 988 $(M+Na)^+$; HRMS (FAB) calcd for $C_{59}H_{83}NNaO_{10}$ $[(M+Na)^+]$ 988.5915, found 988.5895. **64**: $[\alpha]_D^{30}$=+94 (*c* 0.045, MeOH); UV(MeCN) λ_{max} 261 nm (ε 28,000); IR ($CHCl_3$) 3580 (br), 1730, 1695, 1645, 1615, 1455, 1360, 1245, 1090, 970 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6) δ 7.20 (dd, *J*=10.7, 15.1 Hz, 1H), 6.45 [6.42] (dd, *J*=10.7, 15.1 Hz, 1H), 6.31 [6.27] (ddd, *J*=4.9, 10.3, 15.1 Hz, 1H), 5.96 [5.96] (d, *J*=15.1 Hz, 1H), 5.61 (ddd, *J*=4.2, 10.7, 15.1 Hz, 1H), 5.48 (br d, *J*=10.3 Hz, 1H), 5.38 (m, 1H), 5.11 (m, 1H), 4.99 (dd, *J*=8.8, 15.1 Hz, 1H), 4.77 (m, 1H), 3.87 (br d, *J*=4.9 Hz, 1H), 3.68 [3.68] (dd, *J*=7.8, 9.3 Hz, 1H), 3.62–3.43 (m, 7H), 3.37 (ddd, *J*=3.9, 5.9, 9.3 Hz, 1H), 3.30 [3.33] (s, 3H), 3.18 (s, 3H), 3.18 (s, 3H), 3.10 (m, 1H), 2.50–2.32 (m, 3H), 2.36 [2.35] (s, 6H), 2.16 (m, 1H), 2.06–1.98 (m, 2H), 1.94–1.86 (m, 3H), 1.76–1.46 (m, 6H), 1.32 (m, 1H), 1.21 (m, 1H), 1.09 (m, 1H), 1.02–0.99 (m, 9H), 0.95 (d, *J*=6.8 Hz, 3H), 0.74 [0.73] (d, *J*=6.3 Hz, 3H). The counterparts of doubled signals in the ratio of 1:1 are in brackets; MS (FAB) *m/z* 746 $(M+Na)^+$; HRMS (FAB) calcd for $C_{40}H_{69}NNaO_{10}$ $[(M+Na)^+]$ 746.4819, found 746.4819.

3.1.53. Hydrolysis of diol 63. A solution of diol **63** (4.6 mg, 4.8 μmol) in 1,4-dioxane (0.6 mL) and 2 M HCl (0.2 mL) was stirred at 50°C for 5 h and poured into ice-cooled saturated aqueous $NaHCO_3$ (5 mL). The aqueous mixture was extracted with EtOAc (3×10 mL). The extracts were combined, washed with brine (5 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by column chromatography on silica gel (4 g, hexane–acetone 2:1→1:1→1:2) to give **64** (1.5 mg, 44%) as a colorless oil.

3.1.54. Alcohol 65. The experimental procedure was similar to that described for compound **14**. **65** (76% yield, *S*/*R*=1:1): a colorless oil; $[\alpha]_D^{29}$=+22 (*c* 0.75, MeOH); IR ($CHCl_3$) 3520 (br), 1710 (sh), 1645, 1625, 1480, 1360, 1300, 1255, 1035, 1000, 970, 840 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.21 [7.21] (dd, *J*=10.7, 15.1 Hz, 1H), 6.39 [6.41] (dd, *J*=10.7, 15.6 Hz, 1H), 6.25 (m, 1H), 5.90 (d, *J*=15.1 Hz, 1H), 5.55 (ddd, *J*=3.9, 10.2, 14.6 Hz, 1H), 5.38 (m, 1H), 5.29 (m, 1H), 5.12 (dd, *J*=8.8, 14.6 Hz, 1H), 5.07 (dd, *J*=8.8, 14.6 Hz, 1H), 4.86 (td, *J*=6.8, 2.4 Hz, 1H), 3.74 (t, *J*=4.7 Hz, 1H), 3.69 (dd, *J*=7.8, 9.3 Hz, 1H), 3.63 (m, 2H), 3.61 [3.58] (dd, *J*=5.9, 9.3 Hz, 1H), 3.52–3.35 (m, 4H), 3.33 [3.31] (s, 3H), 3.18 (s, 3H), 3.12 (s, 3H), 2.57–2.45 (m, 2H), 2.45–2.24 (m, 4H), 2.36 (s, 3H), 2.36 (s, 3H), 2.10–1.80 (m, 5H), 1.80–1.13 (m, 9H), 1.01 (d, *J*=6.8 Hz, 3H), 1.00 (d, *J*=6.8 Hz, 3H), 1.00–0.94 (m, 3H), 0.91 (s, 18H), 0.78 (d, *J*=6.3 Hz, 3H), 0.14 (s, 3H), 0.11 (s, 3H), 0.09–0.08 (m, 6H). A signal due to OH was not detected. The counterparts of doubled signals in the ratio of 1:1 are in brackets; MS (FAB) *m/z* 974 $(M+Na)^+$; HRMS (FAB) calcd for $C_{52}H_{97}NNaO_{10}Si_2$ $[(M+Na)^+]$ 974.6548, found 974.6539.

3.1.55. Dimethylalanine ester 66. The experimental procedure was similar to that described for compound **29**. **66** (100% yield, *S*/*R*=1:1 as to the trimethylserine part, *S*/*R*=2:1 as to the dimethylalanine part): a colorless oil; $[\alpha]_D^{30}$=+12 (*c* 0.75, MeOH); IR ($CHCl_3$) 1720, 1700, 1645, 1620, 1460, 1280, 840 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.21 [7.22] (dd, *J*=10.7, 15.1 Hz, 1H), 6.40 [6.41] (dd, *J*=10.7, 15.6 Hz, 1H), 6.26 (m, 1H), 5.90 (d, *J*=15.1 Hz, 1H), 5.55 (ddd, *J*=3.9, 10.2, 14.6 Hz, 1H), 5.38 (m, 1H), 5.30 (m, 1H), 5.12 (dd, *J*=8.8, 14.6 Hz, 1H), 5.07 (dd, *J*=8.8, 14.6 Hz, 1H), 4.86 (td, *J*=6.8, 2.4 Hz, 1H), 4.32 [4.33] (dd, *J*=4.4, 11.2 Hz, 1H), 3.88 [3.87] (dd, *J*=7.8, 11.2 Hz, 1H), 3.74 (t, *J*=4.7 Hz, 1H), 3.69 (dd, *J*=7.8, 9.3 Hz, 1H), 3.63 (m, 1H), 3.61 [3.58] (dd, *J*=5.9, 9.3 Hz, 1H), 3.48 (m, 2H), 3.37 (ddd, *J*=3.7, 5.9, 7.8 Hz, 1H), 3.30 [3.31] (dd, *J*=5.9, 7.8 Hz, 3H), 3.27 [3.28] (q, *J*=6.8 Hz, 1H), 3.18 (s, 3H), 3.12 (s, 3H), 2.56–2.45 (m, 2H), 2.45–2.18 (m, 3H), 2.36 [2.36] (s, 6H), 2.28 [2.27] (s, 6H), 2.13–1.75 (m, 5H), 1.65–1.13 (m, 7H), 1.19 [1.20] (d, *J*=6.8 Hz, 3H), 1.04 (d, *J*=6.8 Hz, 6H), 1.00–0.85 (m, 6H), 0.92 (s, 9H), 0.91 (s, 9H), 0.78 (d, *J*=6.8 Hz, 3H), 0.16 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H). The minor counterparts of doubled signals are in brackets; MS (FAB) *m/z* 1073 $(M+Na)^+$; HRMS (FAB) calcd for $C_{57}H_{106}N_2NaO_{11}Si_2$ $[(M+Na)^+]$ 1073.7233, found 1073.7230.

3.1.56. Diol 67. The experimental procedure was similar to that described for compounds **63** and **64**. **67** (78% yield, *S*/*R*=1:1 as to the trimethylserine part, *S*/*R*=2:1 as to the dimethylalanine part): a colorless oil; $[\alpha]_D^{27}$=+66 (*c* 0.10,

MeOH); IR ($CHCl_3$) 3500 (br), 1725, 1695 (sh), 1645, 1620, 1460, 1380, 1240, 1095, 970 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.22 [7.22] (dd, J=10.7, 15.1 Hz, 1H), 6.45 [6.46] (dd, J=10.7, 15.6 Hz, 1H), 6.29 [6.30] (td, J=9.8, 15.6 Hz, 1H), 5.98 [5.98] (d, J=15.1 Hz, 1H), 5.62 (ddd, J=4.4, 10.7, 15.1 Hz, 1H), 5.46 (br d, J=10.3 Hz, 1H), 5.38 (m, 1H), 5.10 (m, 1H), 5.00 (dd, J=9.3, 15.1 Hz, 1H), 4.76 (m, 1H), 4.26 (ddd, J=5.4, 7.8, 11.2 Hz, 1H), 3.90 (ddd, J=5.9, 8.3, 11.2 Hz, 1H), 3.82 (br s, 1H), 3.68 (dd, J=7.8, 9.3 Hz, 1H), 3.58 [3.58] (dd, J=5.4, 9.3 Hz, 1H), 3.50 (m, 3H), 3.37 (dd, J=3.7, 5.4, 7.8 Hz, 1H), 3.33 [3.30] (s, 3H), 3.24 [3.24] (q, J=7.3 Hz, 1H), 3.18 (s, 3H), 3.11 (m, 1H), 3.10 (s, 3H), 2.52–2.40 (m, 2H), 2.35–2.25 (m, 1H), 2.35 [2.36] (s, 6H), 2.28 (s, 6H), 2.25–1.80 (m, 7H), 1.80–1.25 (m, 7H), 1.20 (d, J=6.8 Hz, 3H), 1.04–0.97 (m, 12H), 0.73 [0.72] (d, J=6.3 Hz, 3H). The minor counterparts of doubled signals are in brackets; MS (FAB) m/z 845 $(M+Na)^+$; HRMS (FAB) calcd for $C_{45}H_{78}N_2NaO_{11}$ $[(M+Na)^+]$ 845.5504, found 845.5487.

3.1.57. Olefin 69. The experimental procedure for Julia olefination between **15** and **68** was similar to that described for compound **17** and that for silylation was similar to that given for compound **51**. **69** (70% yield, 20*E*/20*Z*=10:1): a colorless oil; $[\alpha]_D^{31}$=+37.9 (c 0.899, $CHCl_3$); IR ($CHCl_3$) 1720, 1460, 1165, 1090, 1045, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (20*E*-isomer) δ 5.62 (td, J=6.8, 15.6 Hz, 1H), 5.55 (td, J=7.3, 15.6 Hz, 1H), 5.27 (dd, J=8.3, 15.6 Hz, 1H), 5.23 (d, J=8.3, 15.6 Hz, 1H), 4.64 (d, J=11.5 Hz, 1H), 4.58 (d, J=11.5 Hz, 1H), 4.20–4.10 (m, 2H), 3.65 (dd, J=6.8, 6.8 Hz, 1H), 3.64–3.60 (m, 2H), 3.57–3.50 (m, 2H), 3.41 (m, 1H), 3.23 (s, 6H), 2.32–2.27 (m, 2H), 2.16 (s, 3H), 2.10 (m, 1H), 2.00–1.38 (m, 10H), 1.21 (s, 9H), 1.05 (m, 1H), 0.96 (t, J=7.8 Hz, 9H), 0.99–0.87 (m, 10H), 0.90 (s, 9H), 0.60 (q, J=7.8 Hz, 6H), 0.05 (s, 3H), 0.05 (s, 3H); MS (FAB) m/z 825 $(M+Na)^+$; HRMS (FAB) calcd for $C_{43}H_{86}NaO_7SSi_2$ $[(M+Na)^+]$ 825.5530, found 825.5562.

3.1.58. Alcohol 70. The experimental procedure was similar to that described for compound **18**. **70** (93% yield, 20*E*/20*Z*=10:1): a colorless oil; $[\alpha]_D^{32}$=+51.3 (c 1.16, $CHCl_3$); IR ($CHCl_3$) 3470 (br), 1460, 1090, 1050, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (20*E*-isomer) δ 5.62 (td, J=7.3, 15.1 Hz, 1H), 5.55 (td, J=6.8, 15.6 Hz, 1H), 5.30–5.21 (m, 2H), 4.70 (d, J=11.7 Hz, 1H), 4.59 (d, J=11.7 Hz, 1H), 3.82–3.68 (m, 3H), 3.65 (t, J=6.8 Hz, 2H), 3.55 (m, 1H), 3.50 (dd, J=3.4, 4.4 Hz, 1H), 3.42 (m, 1H), 3.24 (s, 3H), 3.23 (s, 3H), 2.50 (br t, J=5.3 Hz, 1H), 2.30 (dt, J=6.8, 6.8 Hz, 2H), 2.21 (s, 3H), 2.11 (m, 1H), 1.98 (m, 1H), 1.90 (ddd, J=7.3, 7.3, 14.6 Hz, 1H), 1.74–1.38 (m, 9H), 1.05 (m, 1H), 0.96 (t, J=7.8 Hz, 9H), 0.90 (s, 9H), 0.90–0.87 (m, 9H), 0.60 (q, J=7.8 Hz, 6H), 0.05 (s, 3H), 0.05 (s, 3H); MS (FAB) m/z 741 $(M+Na)^+$; HRMS (FAB) calcd for $C_{38}H_{78}NaO_6SSi_2$ $[(M+Na)^+]$ 741.4955, found 741.4968.

3.1.59. Aldehyde 71. The experimental procedure was similar to that described for compound **19**. **71** (81% yield, 20*E*/20*Z*=10:1): a colorless oil; $[\alpha]_D^{27}$=+28.8 (c 0.96, $CHCl_3$); IR ($CHCl_3$) 2735, 1720, 1460, 1095, 1095, 975, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) (20*E*-isomer) δ 9.82 (dd, J=2.0, 2.9 Hz, 1H), 5.63 (td, J=6.8, 15.6 Hz, 1H), 5.55 (td, J=7.6, 15.6 Hz, 1H), 5.27 (dd, J=8.3, 15.6 Hz, 1H), 5.24 (dd, J=8.3, 15.6 Hz, 1H), 4.66 (d, J=11.7 Hz, 1H), 4.60 (d, J=11.7 Hz, 1H), 4.05 (ddd, J=3.9, 5.6, 7.6 Hz, 1H), 3.65 (t, J=6.8 Hz, 2H), 3.57 (dd, J=3.7, 3.7 Hz, 1H), 3.53 (m, 1H), 3.42 (ddd, J=6.8, 6.8, 6.8 Hz, 1H), 3.24 (s, 3H), 3.23 (s, 3H), 2.62–2.52 (m, 2H), 2.59 (ddd, J=2.9, 7.3, 16.6 Hz, 1H), 2.53 (ddd, J=2.0, 3.9, 16.6 Hz, 1H), 2.14 (s, 3H), 2.11 (m, 1H), 2.01 (m, 1H), 1.90 (ddd, J=7.3, 7.3, 14.6 Hz, 1H), 1.67–1.38 (m, 7H), 1.05 (m, 1H), 0.96 (t, J=7.8 Hz, 9H), 0.92–0.87 (m, 9H), 0.90 (s, 9H), 0.60 (q, J=7.8 Hz, 6H), 0.05 (s, 3H), 0.05 (s, 3H); MS (FAB) m/z 739 $(M+Na)^+$; HRMS (FAB) calcd for $C_{38}H_{76}NaO_6SSi_2$ $[(M+Na)^+]$ 739.4799, found 739.4799.

3.1.60. α,β,γ,δ-Unsaturated ester 72. The experimental procedure was similar to that described for compound **20**. **72** (89% yield, 4*E*/4*Z*=30:1, 20*E*/20*Z*=10:1): a colorless oil; $[\alpha]_D^{26}$=+0.14 (c 1.04, $CHCl_3$); IR ($CHCl_3$) 1700, 1640, 1620, 1465, 1095, 1045, 970, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) (4*E*,20*E*-isomer) δ 7.26 (dd, J=10.7, 15.1 Hz, 1H), 6.25 (dd, J=10.7, 15.1 Hz, 1H), 6.17 (td, J=7.2, 15.1 Hz, 1H), 5.80 (d, J=15.1 Hz, 1H), 5.62 (td, J=8.3, 15.6 Hz, 1H), 5.55 (td, J=7.3, 15.6 Hz, 1H), 5.27 (dd, J=8.3, 15.6 Hz, 1H), 5.24 (dd, J=8.3, 15.6 Hz, 1H), 4.62 (d, J=11.5 Hz, 1H), 4.59 (d, J=11.5 Hz, 1H), 4.20 (q, J=7.3 Hz, 2H), 3.65 (t, J=6.8 Hz, 2H), 3.65 (m, 1H), 3.59–3.52 (m, 2H), 3.42 (ddd, J=6.8, 6.8, 6.8 Hz, 1H), 3.24 (s, 3H), 3.23 (s, 3H), 2.45 (m, 1H), 2.34–2.28 (m, 3H), 2.15 (s, 3H), 2.12 (m, 1H), 1.92–1.83 (m, 2H), 1.68–1.39 (m, 7H), 1.29 (t, J=7.3 Hz, 3H), 1.05 (m, 1H), 0.96 (t, J=7.8 Hz, 9H), 0.90 (s, 9H), 0.88 (d, J=7.3 Hz, 3H), 0.88 (d, J=6.3 Hz, 3H), 0.85 (d, J=6.8 Hz, 3H), 0.60 (q, J=7.8 Hz, 6H), 0.06 (s, 3H), 0.05 (s, 3H); MS (FAB) m/z 835 $(M+Na)^+$; HRMS (FAB) calcd for $C_{44}H_{84}NaO_7SSi_2$ $[(M+Na)^+]$ 835.5374, found 835.5377.

3.1.61. Hydroxy ester 73. The experimental procedure was similar to that described for compound **21**. **73** (99% yield, 4*E*/4*Z*=30:1, 20*E*/20*Z*=10:1): a colorless oil; $[\alpha]_D^{28}$=−1.99 (c 1.14, $CHCl_3$); IR ($CHCl_3$) 3460 (br), 1700, 1640, 1620, 1460, 1090, 1045, 975, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) (4*E*,20*E*-isomer) δ 7.26 (dd, J=10.7, 15.4 Hz, 1H), 6.25 (dd, J=10.7, 15.4 Hz, 1H), 6.17 (td, J=7.3, 15.4 Hz, 1H), 5.80 (d, J=15.4 Hz, 1H), 5.62 (td, J=7.3, 15.6 Hz, 1H), 5.55 (td, J=7.3, 15.6 Hz, 1H), 5.37 (dd, J=8.3, 15.6 Hz, 1H), 5.24 (dd, J=8.3, 15.6 Hz, 1H), 4.62 (d, J=11.7 Hz, 1H), 4.59 (d, J=11.7 Hz, 1H), 4.20 (q, J=7.3 Hz, 2H), 3.69–3.64 (m, 2H), 3.63 (t, J=3.4 Hz, 1H), 3.59–3.55 (m, 2H), 3.42 (m, 1H), 3.24 (s, 3H), 3.24 (s, 3H), 2.45 (m, 1H), 2.38–2.32 (m, 3H), 2.15 (s, 3H), 2.12 (m, 1H), 1.95–1.82 (m, 2H), 1.66–1.39 (m, 8H), 1.29 (t, J=7.3 Hz, 3H), 1.05 (m, 1H), 0.92–0.88 (m, 6H), 0.90 (s, 9H), 0.85 (d, J=6.8 Hz, 3H), 0.06 (s, 3H), 0.05 (s, 3H); MS (FAB) m/z 721 $(M+Na)^+$; HRMS (FAB) calcd for $C_{38}H_{70}NaO_7SSi$ $[(M+Na)^+]$ 721.4509, found 721.4514.

3.1.62. Lactone 75. The experimental procedure for hydrolysis of **73** was similar to that described for compound **22** to give *seco*-acid **74**. To a solution of crude **74** (10.6 mg obtained from 10.0 mg of **73**, 0.014 mmol) in toluene (20 mL) were added PPh_3 (80 mg, 0.31 mmol) and $(EtOOCN{=})_2$ (0.05 mL, 0.32 mmol) at −10 to −20°C. The mixture was stirred at −10 to −20°C for 4.5 h and at

4°C for 42 h. The mixture was concentrated, and the residual oil was purified by column chromatography on silica gel (5 g, hexane–EtOAc 8:1→6:1→4:1) and preparative TLC (200×100×0.25 mm^3, 2 plates, benzene–EtOAc 6:1) to give **75** (6.0 mg, 64% from **73**) as a colorless oil: $[\alpha]_D^{28}$=+47 (*c* 0.25, $CHCl_3$); IR ($CHCl_3$) 1705, 1645, 1615, 1465, 1255, 1045, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (dd, *J*=10.7, 15.4 Hz, 1H), 6.25 (dd, *J*=10.7, 15.4 Hz, 1H), 6.15 (td, *J*=6.8, 15.4 Hz, 1H), 5.79 (d, *J*=15.4 Hz, 1H), 5.60 (td, *J*=6.8, 15.6 Hz, 1H), 5.38 (td, *J*=7.4, 15.6 Hz, 1H), 5.25 (dd, *J*=8.8, 15.6 Hz, 1H), 5.16 (dd, *J*=8.8, 15.6 Hz, 1H), 4.62 (d, *J*=11.7 Hz, 1H), 4.58 (d, *J*=11.7 Hz, 1H), 4.38 (td, *J*=6.8, 11.2 Hz, 1H), 4.17 (td, *J*=11.2, 3.9 Hz, 1H), 3.68–3.54 (m, 3H), 3.40 (td, *J*=9.0, 4.2 Hz, 1H), 3.24 (s, 3H), 3.23 (s, 3H), 2.45 (m, 2H), 2.34 (m, 2H), 2.17 (s, 3H), 1.97 (m, 2H), 1.82 (m, 1H), 1.68–1.07 (m, 8H), 0.92 (d, *J*=6.8 Hz, 3H), 0.89 (s, 9H), 0.86 (d, *J*=6.8 Hz, 3H), 0.83 (d, *J*=6.3 Hz, 3H), 0.05 (s, 3H), 0.04 (s, 3H); MS (FAB) *m/z* 675 $(M+Na)^+$; HRMS (FAB) calcd for $C_{36}H_{64}NaO_6SSi$ $[(M+Na)^+]$ 675.4091, found 675.4104.

3.1.63. Alcohol 76. The experimental procedure was similar to that described for compound **30**. **76** (91% yield): a colorless oil; $[\alpha]_D^{28}$=+89 (*c* 0.22, $CHCl_3$); IR ($CHCl_3$) 3450 (br), 1730, 1645, 1615, 1465, 1250, 1045, 975, 840 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, *J*=10.2, 15.4 Hz, 1H), 6.25 (dd, *J*=10.2, 15.4 Hz, 1H), 6.18 (td, *J*=7.0, 15.4 Hz, 1H), 5.77 (d, *J*=15.4 Hz, 1H), 5.59 (td, *J*=6.8, 15.6 Hz, 1H), 5.44 (ddd, *J*=6.3, 8.3, 15.6 Hz, 1H), 5.28 (dd, *J*=8.3, 15.6 Hz, 1H), 5.22 (dd, *J*=8.3, 15.6 Hz, 1H), 4.34 (ddd, *J*=5.4, 6.8, 11.2 Hz, 1H), 4.19 (td, *J*=4.4, 11.2 Hz, 1H), 3.80 (t, *J*=2.7 Hz, 1H), 3.66 (m, 1H), 3.56 (td, *J*=5.9, 8.3 Hz, 1H), 3.47 (td, *J*=4.4, 8.3 Hz, 1H), 3.24 (s, 3H), 3.23 (s, 3H), 3.21 (br s, 1H), 2.44 (m, 2H), 2.34 (t, *J*=5.9 Hz, 2H), 2.04 (ddd, *J*=6.8, 6.8, 13.7 Hz, 1H), 1.94 (m, 1H), 1.74–1.36 (m, 8H), 1.07 (m, 1H), 0.95 (d, *J*=6.8 Hz, 3H), 0.91 (s, 9H), 0.88 (d, *J*=6.8 Hz, 3H), 0.83 (d, *J*=6.3 Hz, 3H), 0.10 (s, 3H), 0.08 (s, 3H); MS (FAB) *m/z* 615 $(M+Na)^+$; HRMS (FAB) calcd for $C_{34}H_{60}NaO_6Si$ $[(M+Na)^+]$ 615.4057, found 615.4046.

3.1.64. Trimethylserine ester 77. The experimental procedure was similar to that described for compound **31**. **77** (95% yield, *S*/*R*=1.1:1): a colorless oil; $[\alpha]_D^{25}$=+14 (*c* 0.081, MeOH); IR ($CHCl_3$) 1710, 1645, 1460, 1260, 1095, 975, 835 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.19 (dd, *J*=10.7, 15.4 Hz, 1H), 6.39 [6.39] (dd, *J*=10.7, 15.4 Hz, 1H), 6.22 (m, 1H), 5.85 (d, *J*=15.4 Hz, 1H), 5.63 (td, *J*=7.3, 15.1 Hz, 1H), 5.46 (m, 1H), 5.18–5.13 (m, 2H), 4.90 (m, 1H), 4.36 (m, 1H), 4.11 (m, 1H), 3.71–3.66 (m, 2H), 3.62–3.55 (m, 2H), 3.46 (m, 1H), 3.38 (dd, *J*=4.9, 7.8 Hz, 1H), 3.31 [3.30] (s, 3H), 3.18 (s, 3H), 3.15 (s, 3H), 2.59–2.39 (m, 4H), 2.36 [2.35] (s, 6H), 2.08–1.17 (m, 11H), 0.97 (d, *J*=7.3 Hz, 3H), 0.94 (d, *J*=7.3 Hz, 3H), 0.91 (s, 9H), 0.83 (d, *J*=6.8 Hz, 3H), 0.08 (s, 3H), 0.07 (s, 3H). The minor counterparts of doubled signals in the ratio of 1.1:1 are in brackets; MS (FAB) *m/z* 744 $(M+Na)^+$; HRMS (FAB) calcd for $C_{40}H_{71}NNaO_8Si$ 744.4847, found 744.4828.

3.1.65. Analog 78. The experimental procedure was similar to that described for compound **32**. **78** (85% yield, *S*/*R*=1.1:1): a colorless oil; $[\alpha]_D^{27}$=+61 (*c* 0.054, MeOH); UV (MeCN) λ_{max} 259 nm (ε 25,000); IR ($CHCl_3$) 3510 (br), 1710, 1650, 1620, 1460, 1380, 1270, 1090, 975 cm^{-1}; ^1H NMR (600 MHz, acetone-d_6) δ 7.19 (dd, *J*=10.6, 15.4 Hz, 1H), 6.39 [6.39] (dd, *J*=10.6, 14.7 Hz, 1H), 6.22 (m, 1H), 5.87 (d, *J*=15.4 Hz, 1H), 5.60 (ddd, *J*=4.4, 9.7, 15.4 Hz, 1H), 5.44 (m, 1H), 5.15 (m, 1H), 5.09 (br dd, *J*=9.2, 15.4 Hz, 1H), 4.84 [4.82] (m, 1H), 4.43 [4.44] (ddd, *J*=2.6, 8.4, 14.7 Hz, 1H), 4.05 (ddd, *J*=3.7, 7.3, 14.7 Hz, 1H), 3.67 [3.68] (dd, *J*=7.5, 7.5 Hz, 1H), 3.57 (ddd, *J*=2.2, 5.5, 9.2 Hz, 1H), 3.55–3.49 (m, 2H), 3.44 (dd, *J*=6.0, 12.2 Hz, 1H), 3.38–3.33 (m, 2H), 3.31 [3.29] (s, 3H), 3.17 [3.17] (s, 3H), 3.12 [3.12] (s, 3H), 2.48–2.34 (m, 3H), 2.23 (m, 1H), 2.34 [2.35] (s, 6H), 1.99 (m, 2H), 1.76–1.55 (m, 5H), 1.49 (m, 1H), 1.39 (m, 1H), 1.31 (m, 1H), 1.18 (m, 1H), 1.01 (d, *J*=7.0 Hz, 3H), 0.98 [0.99] (d, *J*=6.6 Hz, 3H), 0.80 [0.79] (d, *J*=7.0 Hz, 3H). The minor counterparts of doubled signals in the ratio of 1.1:1 are in brackets; MS (FAB) *m/z* 630 $(M+Na)^+$; HRMS (FAB) calcd for $C_{34}H_{57}NNaO_8$ 630.3982, found 630.3981.

3.1.66. Lactone 80. To an ice-cooled solution of diene **79** (11.5 mg, 7.56 μmol) in CH_2Cl_2 (0.4 mL) and MeOH (0.8 mL) were added $NiCl_2{\cdot}6H_2O$ (3 mg, 13 μmol) and $NaBH_4$ (6.0 mg, 0.16 mmol). After the mixture was stirred at 0°C for 15 min, acetone (0.2 mL) was added. The mixture was stirred at room temperature for 10 min, diluted with saturated aqueous NH_4Cl (1 mL) and H_2O (1 mL), and extracted with Et_2O (3×10 mL). The combined extracts were washed with brine (2 mL), dried (Na_2SO_4), and concentrated. The residue was purified by preparative TLC on silica gel (200×200×0.25 mm^3, benzene–Et_2O 10:1) to give **80** (8.0 mg, 69%) as a colorless oil: $[\alpha]_D^{28}$=+21 (*c* 0.43, $CHCl_3$); IR ($CHCl_3$) 1725, 1600, 1595, 1460, 1375, 1250, 1170, 1035, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45–7.41 (m, 6H), 7.31–7.20 (m, 9H), 6.89–6.87 (m, 2H), 6.81 (d, *J*=8.3 Hz, 1H), 5.55 (ddd, *J*=3.8, 8.4, 15.1 Hz, 1H), 5.24–5.14 (m, 3H), 4.99 (dd, *J*=2.0, 9.8 Hz, 1H), 4.77 (d, *J*=7.1 Hz, 1H), 4.67 (d, *J*=7.1 Hz, 1H), 4.61 (d, *J*=11.7 Hz, 1H), 4.59 (d, *J*=11.7 Hz, 1H), 4.55 (d, *J*=11.7 Hz, 1H), 4.49 (d, *J*=11.7 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.59–3.38 (m, 6H), 3.23–3.18 (m, 1H), 3.21 (s, 3H), 3.16 (s, 3H), 2.99 (m, 1H), 2.47 (m, 1H), 2.32–2.20 (m, 3H), 2.17 (s, 3H), 2.00 (s, 3H), 2.20–1.74 (m, 5H), 1.74–1.05 (m, 21H), 1.05–0.75 (m, 3H), 1.49 (s, 3H), 0.95 (d, *J*=6.8 Hz, 6H), 0.91 (d, *J*=6.8 Hz, 6H), 0.92 (s, 9H), 0.89 (s, 9H), 0.87 (d, *J*=6.8 Hz, 3H), 0.82 (d, *J*=6.8 Hz, 3H), 0.70 (d, *J*=6.8 Hz, 3H), 0.13 (s, 3H), 0.08 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); MS (FAB) *m/z* 1545 $(M+Na)^+$.

3.1.67. Alcohol 81. The experimental procedure was similar to that described for compound **28**. **81** (79% yield): a colorless oil; $[\alpha]_D^{26}$=+20 (*c* 0.25, $CHCl_3$); IR ($CHCl_3$) 3520 (br), 1725, 1600, 1460, 1375, 1255, 1180, 1155, 835 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.45–7.41 (m, 6H), 7.31–7.21 (m, 9H), 5.54 (ddd, *J*=5.5, 9.3, 15.1 Hz, 1H), 5.24–5.14 (m, 3H), 4.78 (dd, *J*=2.4, 9.8 Hz, 1H), 4.59 (d, *J*=11.7 Hz, 1H), 4.55 (d, *J*=11.7 Hz, 1H), 3.24–3.19 (m, 1H), 3.21 (s, 3H), 3.16 (s, 3H), 3.00 (td, *J*=8.9, 5.9 Hz, 1H), 2.62 (d, *J*=3.9 Hz, 1H, –OH), 2.47 (m, 1H), 2.36–2.20 (m, 3H), 2.17 (s, 3H), 2.08 (s, 3H), 2.20–1.74 (m, 5H), 1.74–1.05 (m, 21H), 1.49 (s, 3H), 0.94 (d, *J*=6.8 Hz, 6H), 1.20–0.84 (m, 33H), 0.82 (d, *J*=

6.8 Hz, 3H), 0.82 (d, J=6.8 Hz, 3H), 0.73 (d, J=6.8 Hz, 3H), 0.12–0.02 (m, 12H); MS (FAB) m/z 1365 $(M+Na)^+$.

3.1.68. Dimethylalanine ester 82. The experimental procedure was similar to that described for compound **29**. **82** (98% yield, S/R=3:1): a colorless oil; $[\alpha]_D^{26}$=+12 (c 0.25, MeOH); IR ($CHCl_3$) 1725, 1600, 1460, 1450, 1375, 1250, 1180, 1155, 835 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.49–7.45 (m, 6H), 7.37–7.32 (m, 6H), 7.29–7.24 (m, 3H), 5.59 (ddd, J=5.4, 8.3, 14.6 Hz, 1H), 5.34 (br t, J=6.6 Hz, 1H), 5.27–5.17 (m, 2H), 4.95 (br t, J=6.1 Hz, 1H), 4.80 (dd, J=2.4, 10.5 Hz, 1H), 4.80 (dd, J=2.4, 10.5 Hz, 1H), 4.64 (s, 2H), 3.72 (m, 1H), 3.59–3.50 (m, 3H), 3.45 (dd, J=5.4, 9.3 Hz, 1H), 3.29–3.21 (m, 1H), 3.19 (q, J=66.8 Hz, 1H), 3.16 (s, 3H), 3.13 (s, 3H), 3.04 (td, J=9.3, 5.9 Hz, 1H), 2.51 (m, 1H), 2.45–2.26 (m, 3H), 2.33 [2.31] (s, 6H), 2.17 (s, 3H), 1.98 [1.96] (s, 3H), 2.18–1.85 (m, 10H), 1.51 (s, 3H), 1.76–1.44 (m, 13H), 1.44–1.23 (m, 6H), 1.26 [1.21] (d, J=6.8 Hz, 3H), 1.05 (d, J=6.8 Hz, 3H), 1.02 (d, J=6.8 Hz, 3H), 0.99 (d, J=6.8 Hz, 3H), 0.96 (s, 9H), 0.94 (d, J=6.8 Hz, 3H), 0.92 (s, 9H), 0.89 (d, J=6.8 Hz, 3H), 0.87 (d, J=6.8 Hz, 3H), 0.71 (d, J=6.8 Hz, 3H), 0.15 (s, 3H), 0.17 (s, 3H),0.14 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H). The minor counterparts of doubled signals in the ratio of 3:1 are in brackets; MS (FAB) m/z 1464 $(M+Na)^+$.

3.1.69. Alcohol 83. The experimental procedure was similar to that described for compound **30**. **83** (95% yield, S/R=3:1): a colorless oil; $[\alpha]_D^{26}$=+5.7 (c 0.24, MeOH); IR ($CHCl_3$) 3345 (br), 1725, 1600, 1460, 1450, 1250, 840 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.48–7.44 (m, 6H), 7.35–7.31 (m, 6H), 7.28–7.23 (m, 3H), 5.57 (td, J=6.8, 15.6 Hz, 1H), 5.34 (t, J=7.1 Hz, 1H), 5.27–5.18 (m, 2H), 4.93 (m, 1H), 4.78 (dd, J=2.4, 9.8 Hz, 1H), 3.96 (t, J=3.4 Hz, 1H), 3.58–3.48 (m, 2H), 3.48–3.40 (m, 2H), 3.31 (d, J=4.9 Hz, 1H, –OH), 3.27–3.14 (m, 2H), 3.17 (s, 3H), 3.10 (s, 3H), 3.03 (td, J=8.8, 5.4 Hz, 1H), 2.51–1.85 (m, 6H), 2.32 [2.30] (s, 6H), 1.96 [1.95] (s, 3H), 1.73–1.15 (m, 27H), 1.49 (s, 3H), 1.24 [1.19] (d, J=7.3 Hz, 3H), 1.04 (d, J=6.8 Hz, 3H), 1.01 (d, J=6.8 Hz, 3H), 0.98 (d, J=6.8 Hz, 3H), 0.95 (s, 9H), 0.92 (d, J=6.8 Hz, 3H), 0.91 (s, 9H), 0.88 (d, J=6.8 Hz, 3H), 0.84 (d, J=6.8 Hz, 3H), 0.70 (d, J=6.8 Hz, 3H), 0.15 (s, 3H), 0.13 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H). The minor counterparts of doubled signals in the ratio of 3:1 are in brackets; MS (FAB) m/z 1404 $(M+Na)^+$.

3.1.70. Trimethylserine ester 84. The experimental procedure was similar to that described for compound **31**. **84** (83% yield, S/R=1.2:1 as to the trimethylserine part, S/R=3:1 as to the dimethylalanine part): a colorless oil; $[\alpha]_D^{25}$=+8.6 (c 0.19, MeOH); IR ($CHCl_3$) 1730, 1700 (sh), 1655, 1460, 1375, 1250, 1095, 970, 835 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.48–7.44 (m, 6H), 7.36–7.31 (m, 6H), 7.28–7.23 (m, 3H), 5.56 (m, 1H), 5.34 (t, J=6.6 Hz, 1H), 5.26–5.18 (m, 2H), 4.93 (m, 1H), 4.83 (m, 1H), 4.78 (dd, J=2.4, 10.2 Hz, 1H), 3.68 [3.68][b] (dd, J=7.3, 9.3 Hz, 1H), 3.64–3.49 (m, 4H), 3.46 (dd, J=4.9, 10.2 Hz, 1H), 3.36 (ddd, J=3.9, 5.4, 7.3 Hz, 1H), 3.31 [3.30][a] (s, 3H), 3.28–3.14 (m, 2H), 3.17 (s, 3H), 3.11 (s, 3H), 3.03 (td, J=8.8, 5.4 Hz, 1H), 2.50 (m, 1H), 2.40–2.15 (m, 4H), 2.37 [2.36][b] (s, 6H), 2.32 [2.30][a] (s, 3H), 2.15–1.80 (m, 10H), 1.96 [1.95][a] (s, 3H), 1.80–1.42 (m, 13H), 1.51 (s, 3H), 1.42–1.10 (m, 11H), 1.24 [1.19][b] (d, J=7.3 Hz, 3H), 1.04 (d, J=6.8 Hz, 3H), 1.01 (d, J=6.8 Hz, 3H), 0.97 (d, J=6.8 Hz, 3H), 0.95 (s, 9H), 0.95–0.91 (m, 3H), 0.91 (s, 9H), 0.88 (d, J=6.8 Hz, 3H), 0.70 (d, J=6.8 Hz, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H). The minor counterparts of doubled signals in the ratios of 3:1 (superscript a) and 1.2:1 (superscript b) are in brackets.

3.1.71. Analog 85. The experimental procedure was similar to that described for compound **32**. **85** (85% yield, S/R= 1.2:1 as to the trimethylserine part, S/R=3:1 as to the dimethylalanine part): a colorless oil; $[\alpha]_D^{26}$=+16 (c 0.13, MeOH); IR ($CHCl_3$) 3500 (br), 1725, 1460, 1375, 1240, 1090, 970 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 5.60 (td, J=6.8, 14.6 Hz, 1H), 5.43–5.35 (m, 2H), 5.23 (dd, J=7.3, 14.6 Hz, 1H), 4.97–4.82 (m, 2H), 4.79 (dd, J=2.4, 9.8 Hz, 1H), 3.71–3.43 (m, 8H), 3.35 (m, 1H), 3.30 [3.29][a] (s, 3H), 3.30 [3.29][b] (s, 3H), 3.11 [3.11][b] (s, 3H), 2.51 (m, 1H), 2.38–2.28 (m, 14H), 2.13–1.98 (m, 9H), 2.00 [2.01][a] (s, 3H), 1.98–1.47 (m, 15H), 1.53 [1.51][b] (s, 3H), 1.41–1.10 (m, 10H), 1.01–0.85 (m, 21H). Signals of three protons (3× OH) were not observed. The minor counterparts of doubled signals in the ratios of 3:1 (superscript a), and 1.2:1 (superscript b) are in brackets; MS (FAB) m/z 1063 $(M+Na)^+$; HRMS (FAB) calcd for $C_{57}H_{104}N_2NaO_{14}$ $[(M+Na)^+]$ 1063.7385, found 1063.7440.

3.1.72. Diacetate 87. A mixture of diol **86** (5.5 mg, 9.3 μmol), DMAP (1.9 mg, 15 μmol), Ac_2O (0.16 mL), and pyridine (0.16 mL) was stirred at room temperature for 3 h and concentrated in vacuo. The residue was purified by column chromatography on silica gel (0.5 g, hexane–Et_2O 4:1→3:1) to give **87** (6.7 mg, 100%) as a colorless oil: $[\alpha]_D^{31}$=+7.8 (c 0.34, $CHCl_3$); IR ($CHCl_3$) 1725, 1460, 1370, 1255, 1095, 1080, 1025 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 5.28 (ddd, J=2.0, 6.9, 7.3 Hz, 1H), 4.91 (d, J=4.6 Hz, 1H), 4.10–3.96 (m, 3H), 3.55 (dd, J=2.6, 7.3 Hz, 1H), 3.35 (dd, J=6.6, 9.6 Hz, 1H), 3.30 (s, 3H), 2.23 (m, 1H), 2.08 (dd, J=7.6, 12.9 Hz, 1H), 2.04 (s, 6H), 1.90–1.36 (m, 10H), 1.09 (d, J=6.6 Hz, 3H), 0.96 (t, J=7.9 Hz, 18H), 0.93 (d, J=6.9 Hz, 3H), 0.90 (d, J=7.3 Hz, 3H), 0.81 (d, J=6.9 Hz, 3H), 0.62 (q, J=7.9 Hz, 6H), 0.60 (q, J=7.9 Hz, 6H); MS (FAB) m/z 697 $(M+Na)^+$; HRMS (FAB) calcd for $C_{35}H_{70}NaO_8Si_2$ $[(M+Na)^+]$ 697.4507, found 697.4512.

3.1.73. Tetraol 88. A solution of diacetate **87** (8.8 mg, 13 μmol) in DME (0.56 mL) and 1 M HCl (0.14 mL) was stirred at room temperature for 3.5 h. The reaction mixture was diluted with saturated aqueous $NaHCO_3$ (2 mL) and extracted with EtOAc (3×2 mL). The combined extracts were washed with brine (1 mL), dried (Na_2SO_4), and concentrated. The residue was purified by preparative TLC on silica gel (200×100×0.25 mm^3, 2 plates, hexane–acetone 3:2) to give a diastereomeric mixture of hemiacetals (4.3 mg) as a colorless oil. The mixture was used in the next experiment without purification.

To an ice-cooled solution of the mixture of hemiacetals (1.4 mg) in EtOH (0.2 mL) was added $NaBH_4$ (0.8 mg, 0.02 mmol). The mixture was stirred at 0°C for 6 h, diluted with saturated aqueous NH_4Cl (1 mL), and extracted with EtOAc (4×2 mL). The combined extracts were washed with brine (1 mL), dried (Na_2SO_4), and concentrated. The residue

was purified by preparative TLC on silica gel (100×100×0.25 mm^3, 2 plates, hexane–acetone 1:1) to give **88** (1.1 mg, 60% from **87**) as a colorless oil: $[\alpha]_D^{23}=-15.8$ (*c* 0.091, $CHCl_3$); IR ($CHCl_3$) 3380 (br), 1725, 1455, 1380, 1260, 1020 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.29 (br t, *J*=8.3 Hz, 1H), 4.75 (d, *J*=4.9 Hz, 1H, –OH), 4.60 (br s, 1H, –OH), 4.40 (br s, 1H, –OH), 4.23 (ddd, *J*=5.9, 8.3, 11.2 Hz, 1H), 4.14 (ddd, *J*=5.4, 5.4, 11.2 Hz, 1H), 4.04 (m, 1H), 3.71 (dt, *J*=2.4, 10.2 Hz, 1H), 3.63 (d, *J*=7.8 Hz, 1H, –OH), 3.48 (m, 1H), 3.14 (m, 1H), 3.01 (dd, *J*=2.4, 10.4 Hz, 1H), 2.12 (s, 3H), 2.06 (s, 3H), 2.08–1.95 (m, 2H), 1.90–1.47 (m, 9H), 1.07 (d, *J*=7.3 Hz, 3H), 1.06 (d, *J*=6.8 Hz, 3H), 0.90 (m, 1H), 0.84 (d, *J*=6.4 Hz, 3H), 0.82 (d, *J*=6.4 Hz, 3H); MS (FAB) *m/z* 457 $(M+Na)^+$; HRMS (FAB) calcd for $C_{22}H_{42}NaO_8$ $[(M+Na)^+]$ 457.2777, found 457.2765.

3.1.74. Analog 89. A solution of tetraol **88** (1.7 mg, 3.9 μmol) in a 0.23 M solution of NaOMe in MeOH (0.07 mL, 16 μmol) was stirred at room temperature for 5 h. Amberlite IRC-50 (H^+ form, 20 mg) was added, and the mixture was stirred for 20 min and then passed through a column of Amberlite IRC-50 (H^+ form, 100 mg). The resin was washed with MeOH (10 mL), and the eluate and washings were combined and concentrated. The residue was purified by preparative TLC on silica gel (130×100×0.25 mm^3, CH_2Cl_2–acetone–MeOH 4:4:1) to give **89** (1.5 mg, 100%) as a colorless oil: $[\alpha]_D^{29}=-3.6$ (*c* 0.13, MeOH); IR (film) 3340, 2930, 1455, 1380, 1260, 1055 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 4.39 (d, *J*=5.2 Hz, 1H), 4.17 (m, 1H), 4.11 (d, *J*=5.6 Hz, 1H), 4.09 (d, *J*=3.6 Hz, 1H), 3.94 (m, 1H), 3.85 (d, *J*=4.4 Hz, 1H), 3.78–3.63 (m, 5H), 3.56 (m, 1H), 3.34 (m, 2H), 2.05–1.61 (m, 7H), 1.58–1.49 (m, 2H), 1.46–1.36 (m, 2H), 1.08 (m, 1H), 0.92 (d, *J*=6.8 Hz, 3H), 0.91 (d, *J*=6.8 Hz, 6H), 0.91 (d, *J*=6.8 Hz, 3H); MS (FAB) *m/z* 373 $(M+Na)^+$; HRMS (FAB) calcd for $C_{18}H_{38}NaO_6$ $[(M+Na)^+]$ 373.2566, found 373.2560.

3.1.75. TBDPS ether 90. A solution of diol **86** (23.3 mg, 39.5 μmol), TBDPSCl (0.015 mL, 58 μmol), and imidazole (8.1 mg, 0.13 mmol) in DMF (0.2 mL) was stirred at room temperature for 50 min. After ice (2 g) and H_2O (1 mL) were added, the mixture was stirred at room temperature for 1 h and extracted with Et_2O (3×3 mL). The combined extracts were washed with brine (3 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (2 g, hexane–Et_2O 4:1→2:1) to give **90** (33.0 mg, 100%) as a colorless oil: $[\alpha]_D^{31}=+14.9$ (*c* 1.67, $CHCl_3$); IR ($CHCl_3$) 3500 (br), 1460, 1425, 1415, 1380, 1235, 1215, 1110, 1080, 1025, 1010 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.69–7.65 (m, 4H), 7.42–7.33 (m, 6H), 4.91 (d, *J*=5.0 Hz, 1H), 3.94 (m, 1H), 3.84 (m, 1H), 3.64 (t, *J*=6.9 Hz, 2H), 3.56 (dd, *J*=6.9, 8.3 Hz, 1H), 3.55 (dd, *J*=1.3, 7.9 Hz, 1H), 3.33 (s, 3H), 2.67 (m, 1H, –OH), 2.24 (m, 1H), 2.08 (dd, *J*=6.9, 12.9 Hz, 1H), 1.91–1.28 (m, 10H), 1.06 (d, *J*=6.6 Hz, 3H), 1.05 (s, 9H), 1.04 (d, *J*=4.6 Hz, 3H), 0.95 (d, *J*=7.3 Hz, 3H), 0.91 (t, *J*=7.6 Hz, 18H), 0.78 (d, *J*=7.3 Hz, 3H), 0.57 (q, *J*=7.3 Hz, 6H), 0.54 (q, *J*=7.3 Hz, 6H); MS (FAB) *m/z* 851 $(M+Na)^+$.

3.1.76. DMBOM ether 91. To a solution of TBDPS ether **90** (33.0 mg, 39.5 μmol) in CH_2Cl_2 (0.34 mL) were added *i*-Pr_2NEt (0.34 mL, 0.20 mmol) and a 1 M solution of DMBOM–Cl[3d,16] in CH_2Cl_2 (0.52 mL, 0.52 mmol). After the mixture was stirred at room temperature for 13 h, MeOH (2 mL) and $NaHCO_3$ (19 mg) were added. The mixture was stirred at room temperature for 10 h, diluted with H_2O (3 mL), and extracted with hexane (5×3 mL). The combined extracts were washed successively with saturated aqueous $NaHCO_3$ (5 mL), H_2O (5 mL), and brine (5 mL), and then dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography on alumina (5 g, hexane–EtOAc 15:1→10:1→7:1) and preparative TLC on silica gel (200×100×0.25 mm^3, 4 plates, hexane–Et_2O 1:1) to give **91** (37.4 mg, 94%) as a colorless oil: $[\alpha]_D^{31}=+7.7$ (*c* 0.87, $CHCl_3$); IR ($CHCl_3$) 1595, 1515, 1465, 1265, 1240, 1215, 1095, 1030 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.69–7.60 (m, 4H), 7.45–7.33 (m, 6H), 6.91 (d, *J*=7.9 Hz, 1H), 6.90 (s, 1H), 6.81 (d, *J*=7.9 Hz, 1H), 4.87 (d, *J*=4.6 Hz, 1H), 4.82 (s, 2H), 4.61 (d, *J*=11.2 Hz, 1H), 4.55 (d, *J*=11.2 Hz, 1H), 4.03 (ddd, *J*=0.7, 6.6, 6.6 Hz, 1H), 3.91 (m, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.60 (t, *J*=6.9 Hz, 2H), 3.59 (dd, *J*=3.3, 6.9 Hz, 1H), 3.53 (dd, *J*=2.0, 7.3 Hz, 1H), 3.22 (s, 3H), 2.25 (m, 1H), 2.09 (dd, *J*=7.3, 12.5 Hz, 1H), 1.78–1.32 (m, 10H), 1.10 (d, *J*=6.6 Hz, 3H), 1.04 (s, 9H), 0.93–0.85 (m, 6H), 0.90 (t, *J*=7.6 Hz, 18H), 0.74 (d, *J*=6.9 Hz, 3H), 0.55 (q, *J*=7.6 Hz, 6H), 0.53 (q, *J*=7.6 Hz, 6H); MS (FAB) *m/z* 1031 $(M+Na)^+$.

3.1.77. Diol 92. The experimental procedure was similar to that described for compound **21**. **92** (90% yield): a colorless oil; $[\alpha]_D^{30}=+7.5$ (*c* 1.03, $CHCl_3$); IR ($CHCl_3$) 3470 (br), 1595, 1515, 1465, 1430, 1380, 1265, 1240, 1210, 1100, 1030 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.65 (m, 4H), 7.46–7.38 (m, 6H), 6.94 (s, 1H), 6.92 (d, *J*=8.3 Hz, 1H), 6.82 (d, *J*=8.3 Hz, 1H), 4.89 (d, *J*=4.4 Hz, 1H), 4.87 (d, *J*=6.8 Hz, 1H), 4.84 (d, *J*=6.8 Hz, 1H), 4.62 (d, *J*=11.2 Hz, 1H), 4.58 (d, *J*=11.2 Hz, 1H), 4.20 (m, 1H), 4.08 (m, 1H), 3.92–3.81 (m, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 3.81 (br s, 1H, –OH), 3.57 (dd, *J*=6.8, 9.8 Hz, 1H), 3.34 (m, 1H), 3.29 (s, 3H), 2.24 (m, 1H), 2.09 (dd, *J*=7.2, 12.8 Hz, 1H), 1.91 (ddq, *J*=9.6, 14.8, 4.8 Hz, 1H), 1.80 (ddq, *J*=2.0, 6.8, 6.8 Hz, 1H), 1.70–1.59 (m, 7H), 1.45 (m, 1H), 1.10 (d, *J*=6.8 Hz, 3H), 1.04 (s, 9H), 0.94 (d, *J*=6.0 Hz, 3H), 0.90 (d, *J*=6.8 Hz, 3H), 0.89 (d, *J*=6.8 Hz, 3H); MS (FAB) *m/z* 803 $(M+Na)^+$.

3.1.78. Silyl ether 93. To an ice-cooled solution of diol **92** (20.2 mg, 25.9 μmol) in CH_2Cl_2 were added 2,6-lutidine (0.015 mL, 0.12 mmol) and *t*-$BuMe_2SiOTf$ (0.022 mL, 0.097 mmol). After the mixture was stirred at 0°C for 1.5 h, 2,6-lutidine (0.015 mL, 0.12 mmol) and *t*-$BuMe_2$-SiOTf (0.022 mL, 0.097 mmol) were added. After the mixture was stirred at 0°C for 1 h, the reaction was quenched by adding ice (3 g), and the mixture was extracted with Et_2O (3×3 mL). The combined extracts were washed with brine (3 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (1.5 g, hexane–Et_2O 5:1→3:1→1:1) to give **93** (26.2 mg, 100%) as a colorless oil: $[\alpha]_D^{31}=+6.3$ (*c* 1.41, $CHCl_3$); IR ($CHCl_3$) 1595, 1515, 1465, 1425, 1380, 1360, 1255, 1215, 1155, 1140, 1095, 1080, 1030 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.67–7.63 (m, 4H), 7.44–7.33 (m, 6H), 6.91 (d, *J*=7.9 Hz, 1H), 6.89 (s, 1H), 6.82 (d, *J*=7.9 Hz, 1H), 4.88 (d, *J*=4.6 Hz, 1H), 4.82 (s, 2H), 4.61 (d,

J=11.6 Hz, 1H), 4.55 (d, J=11.6 Hz, 1H), 4.04 (ddd, J=1.0, 6.3, 6.3 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.85 (m, 1H), 3.66 (t, J=6.9 Hz, 2H), 3.58 (dd, J=6.6, 9.9 Hz, 1H), 3.52 (dd, J=1.7, 6.9 Hz, 1H), 3.24 (s, 3H), 2.24 (m, 1H), 2.09 (dd, J=7.6, 12.5 Hz, 1H), 1.86–1.71 (m, 2H), 1.66–1.39 (m, 8H), 1.10 (d, J=6.6 Hz, 3H), 1.04 (s, 9H), 0.93 (d, J=6.9 Hz, 3H), 0.87 (d, J=7.3 Hz, 3H), 0.84 (s, 9H), 0.83 (s, 9H), 0.77 (d, J=7.3 Hz, 3H), 0.01 (s, 3H), 0.00 (s, 3H), −0.01 (s, 3H), −0.02 (s, 3H); MS (FAB) m/z 1031 $(M+Na)^+$.

3.1.79. Diol 94. The experimental procedure was similar to that described for compound **88**. **94** (72% yield): a colorless oil; $[\alpha]_D^{30}$=−19.3 (c 0.995, $CHCl_3$); IR ($CHCl_3$) 3440 (br), 1595, 1520, 1460, 1425, 1395, 1360, 1260, 1215, 1160, 1140, 1110, 1080, 1030 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.67–7.63 (m, 4H), 7.44–7.33 (m, 6H), 6.88–6.80 (m, 3H), 4.80 (d, J=6.9 Hz, 1H), 4.75 (d, J=6.9 Hz, 1H), 4.64 (d, J=11.9 Hz, 1H), 4.50 (d, J=11.9 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.88–3.87 (m, 2H), 3.74–3.53 (m, 4H), 3.66 (t, J=6.9 Hz, 2H), 3.52 (dd, J=1.3, 5.9 Hz, 1H), 3.45 (dd, J=4.0, 8.3 Hz, 1H), 1.96–1.26 (m, 12H), 1.04 (s, 9H), 0.99 (d, J=6.9 Hz, 3H), 0.92 (d, J=6.9 Hz, 3H), 0.90 (s, 9H), 0.87 (d, J=7.3 Hz, 3H), 0.84 (s, 9H), 0.83 (s, 9H), 0.80 (d, J=7.3 Hz, 3H), 0.01 (s, 6H), −0.01 (s, 3H), −0.02 (s, 3H); MS (FAB) m/z 1019 $(M+Na)^+$.

3.1.80. Trityl ether 95. A solution of diol **94** (16.0 mg, 16.1 μmol) and TrCl (18 mg, 64 μmol) in pyridine (0.17 mL) was stirred at 50°C for 13.5 h. The mixture was diluted with saturated aqueous $NaHCO_3$ (1 mL), stirred at room temperature for 1.5 h, and extracted with Et_2O (3×2 mL). The combined extracts were washed with brine (2 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (1.5 g, hexane–Et_2O 5:1→3:1→1:1) to give **95** (18.6 mg, 93%) as a colorless oil: $[\alpha]_D^{30}$=−3.3 (c 0.36, $CHCl_3$); IR ($CHCl_3$) 3490 (br), 1595, 1520, 1460, 1450, 1425, 1385, 1360, 1260, 1220, 1210, 1155, 1140, 1110, 1075, 1025, 1005 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.67–7.63 (m, 4H), 7.46–7.18 (m, 21H), 6.88–6.78 (m, 3H), 4.80 (d, J=6.9 Hz, 1H), 4.74 (d, J=6.9 Hz, 1H), 4.64 (d, J=11.5 Hz, 1H), 4.49 (d, J=11.5 Hz, 1H), 3.91–3.85 (m, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.67 (t, J=6.9 Hz, 2H), 3.54 (dd, J=1.7, 6.3 Hz, 1H), 3.44 (m, 1H), 3.44 (br s, 1H, –OH), 3.24 (m, 1H), 3.00 (m, 1H), 1.90–1.41 (m, 12H), 1.05 (s, 9H), 0.94 (d, J=6.9 Hz, 3H), 0.89 (d, J=6.9 Hz, 3H), 0.84 (s, 9H), 0.83 (d, J=7.3 Hz, 3H), 0.83 (s, 9H), 0.80 (d, J=7.3 Hz, 3H), 0.02 (s, 3H), 0.01 (s, 3H), 0.00 (s, 3H), −0.01 (s, 3H); MS (FAB) m/z 1261 $(M+Na)^+$.

3.1.81. Acetate 96. A solution of trityl ether **95** (18.6 mg, 15.0 μmol) and DMAP (0.9 mg, 7 μmol) in Ac_2O (0.13 mL) and pyridine (0.26 mL) was stirred at room temperature for 22 h. The mixture was concentrated in vacuo and purified by column chromatography on silica gel (1 g, hexane–Et_2O 4:1→2:1) to give **96** (16.7 mg, 87%) as a colorless oil: $[\alpha]_D^{30}$=+5.5 (c 1.0, $CHCl_3$); IR ($CHCl_3$) 1725, 1595, 1520, 1460, 1385, 1255, 1215, 1160, 1140, 1110, 1070, 1030 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66–7.63 (m, 4H), 7.45–7.20 (m, 21H), 6.89–6.79 (m, 3H), 4.98 (dd, J=2.4, 9.8 Hz, 1H), 4.76 (d, J=7.3 Hz, 1H), 4.67 (d, J=7.3 Hz, 1H), 4.61 (d, J=11.7 Hz, 1H), 4.49 (d, J=11.7 Hz, 1H), 3.88 (m, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.66 (t, J=6.8 Hz, 2H), 3.51 (dd, J=2.4, 6.8 Hz, 1H), 3.39 (m, 1H), 3.20 (m, 1H), 2.98 (ddd, J=5.9, 8.8, 8.8 Hz, 1H), 1.96 (s, 3H), 2.36–1.40 (m, 12H), 1.04 (s, 9H), 0.95 (d, J=7.3 Hz, 3H), 0.94 (d, J=6.8 Hz, 3H), 0.86 (s, 9H), 0.83 (s, 9H), 0.79 (d, J=6.8 Hz, 3H), 0.69 (d, J=6.8 Hz, 3H), 0.03 (s, 3H), 0.01 (s, 3H), −0.01 (s, 3H), −0.02 (s, 3H); MS (FAB) m/z 1303 $(M+Na)^+$.

3.1.82. Alcohol 97. A solution of acetate **96** (21.2 mg, 16.6 μmol) in HCOOH (0.08 mL) and Et_2O (0.12 mL) was stirred at room temperature for 30 min. The mixture was poured into ice-cooled saturated aqueous $NaHCO_3$ (3 mL), and the aqueous mixture was extracted with Et_2O (5×3 mL). The combined extracts were washed with brine (5 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (1 g, hexane–Et_2O 3:1→2:1→1:1→1:3) to give **97** (11.8 mg, 68%) as a colorless oil, along with **96** (1.7 mg, 8%). **97**: $[\alpha]_D^{30}$=+3.7 (c 0.82, $CHCl_3$); IR ($CHCl_3$) 3500 (br), 1725, 1595, 1520, 1465, 1430, 1385, 1255, 1215, 1160, 1140, 1110, 1030 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.68–7.63 (m, 4H), 7.44–7.33 (m, 6H), 6.87 (d, J=8.6 Hz, 1H), 6.86 (s, 1H), 6.81 (d, J=8.6 Hz, 1H), 4.98 (dd, J=2.6, 9.6 Hz, 1H), 4.75 (d, J=6.9 Hz, 1H), 4.66 (d, J=6.9 Hz, 1H), 4.59 (d, J=11.9 Hz, 1H), 4.50 (d, J=11.9 Hz, 1H), 3.90–3.86 (m, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 3.80–3.59 (m, 2H), 3.66 (t, J=6.9 Hz, 2H), 3.50 (dd, J=2.6, 6.6 Hz, 1H), 3.49 (m, 1H), 2.01 (s, 1H), 2.03–1.34 (m, 12H), 1.04 (s, 9H), 0.92 (d, J=6.9 Hz, 3H), 0.90 (d, J=6.9 Hz, 3H), 0.85 (s, 9H), 0.84 (d, J=6.9 Hz, 3H), 0.83 (s, 9H), 0.79 (d, J=6.9 Hz, 3H), 0.02 (s, 3H), 0.01 (s, 3H), −0.02 (s, 6H); MS (FAB) m/z 1061 $(M+Na)^+$.

3.1.83. Aldehyde 98. To a solution of alcohol **97** (6.2 mg, 6.0 μmol) in CH_2Cl_2 (0.14 mL) were added pyridine (0.014 mL, 0.17 mmol) and the Dess–Martin periodinane, $C_6H_4(COO)I(OAc)_3$ (6.9 mg, 16 μmol). After the mixture was stirred at room temperature for 40 min, saturated aqueous $NaHCO_3$ (1 mL) and saturated aqueous $Na_2S_2O_3$ (1 mL) were added. The aqueous mixture was stirred at room temperature for 20 min and extracted with Et_2O (3×3 mL). The combined extracts were washed with brine (3 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (0.3 g, hexane–EtOAc 5:1→3:1→1:1) to give **98** (5.5 mg, 89%) as a colorless oil: $[\alpha]_D^{29}$=+4.3 (c 0.45, $CHCl_3$); IR ($CHCl_3$) 1725, 1595, 1515, 1460, 1430, 1385, 1250, 1220, 1160, 1140, 1110, 1075, 1030 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 9.75 (m, 1H), 7.67–7.63 (m, 4H), 7.43–7.33 (m, 6H), 6.87 (d, J=8.6 Hz, 1H), 6.86 (s, 1H), 6.81 (d, J=8.6 Hz, 1H), 5.00 (dd, J=3.0, 9.2 Hz, 1H), 4.75 (d, J=6.9 Hz, 1H), 4.66 (d, J=6.9 Hz, 1H), 4.60 (d, J=11.6 Hz, 1H), 4.49 (d, J=11.6 Hz, 1H), 3.87 (m, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.66 (t, J=6.9 Hz, 2H), 3.50 (dd, J=2.0, 6.3 Hz, 1H), 3.44 (ddd, J=0.8, 7.3, 7.3 Hz, 1H), 2.47–2.42 (m, 2H), 2.28 (ddd, J=2.3, 9.6, 16.8 Hz, 1H), 2.01 (s, 3H), 1.88–1.40 (m, 9H), 1.04 (s, 9H), 0.96 (d, J=6.6 Hz, 3H), 0.92 (d, J=6.6 Hz, 3H), 0.89 (d, J=6.6 Hz, 3H), 0.85 (s, 9H), 0.83 (s, 9H), 0.79 (d, J=6.9 Hz, 3H), 0.02 (s, 3H), 0.01 (s, 3H),−0.01 (s, 6H); MS (FAB) m/z 1059 $(M+Na)^+$.

3.1.84. Enamide 99. A solution of aldehyde **98** (4.4 mg,

4.2 μmol), *N*-methylformamide (0.06 mL, 1.0 mmol), pyridinium *p*-toluenesulfonate (2.1 mg, 8.4 μmol), and hydroquinone (0.9 mg, 8 μmol) in benzene (3.2 mL) was refluxed for 18 h with the continuous removal of water by use of molecular sieves 3 Å. Triethylamine (0.06 mL) and saturated aqueous $NaHCO_3$ (3 mL) were added, and the aqueous mixture was extracted with Et_2O (3×3 mL). The combined extracts were washed with brine (3 mL), dried (Na_2SO_4), and concentrated. The residue was purified by preparative TLC on silica gel (200×100×0.25 mm^3, hexane–EtOAc 3:2) and by column chromatography on silica gel (0.3 g, hexane–EtOAc 5:1→3:1→1:1) to give **99** (2.3 mg, 51%) as a colorless oil: $[\alpha]_D^{30}=-10.9$ (*c* 0.237, $CHCl_3$); IR ($CHCl_3$) 1725, 1690, 1655, 1595, 1515, 1460, 1430, 1375, 1255, 1220, 1160, 1140, 1110, 1080, 1030 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 [8.03] (s, 1H), 7.66–7.63 (m, 4H), 7.43–7.34 (m, 6H), 7.00–6.80 (m, 3H), 6.47 [7.16] (d, *J*=14.0 Hz, 1H), 5.05–4.98 (m, 2H), 4.75 [4.74] (d, *J*=6.8 Hz, 1H), 4.64 (d, *J*=6.8 Hz, 1H), 4.59 (d, *J*=11.6 Hz, 1H), 4.49 [4.48] (d, *J*=11.6 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.86 (m, 1H), 3.65 (t, *J*=6.8 Hz, 2H), 3.49 (dd, *J*=2.4, 6.4 Hz, 1H), 3.45 (m, 1H), 2.97 (s, 3H), 2.54 (m, 1H), 2.04 (s, 3H), 1.85–1.25 (m, 9H), 1.05–1.01 (m, 3H), 1.04 (s, 9H), 0.91 (d, *J*=6.8 Hz, 3H), 0.87 (d, *J*=6.8 Hz, 3H), 0.82 (s, 18H), 0.78 (d, *J*=6.8 Hz, 3H), 0.00 [−0.01] (s, 6H), −0.02 (s, 6H). The minor counterparts of doubled signals in the ratio of 2:1 due to the rotamers are in brackets; MS (FAB) *m/z* 1100 $(M+Na)^+$.

3.1.85. Alcohol 100. The experimental procedure was similar to that described for compound **28**. **100** (86% yield): a colorless oil; $[\alpha]_D^{30}=-22.0$ (*c* 0.102, $CHCl_3$); IR ($CHCl_3$) 3500 (br), 1715, 1695, 1655, 1470, 1460, 1425, 1390, 1370, 1255, 1215, 1110, 1080 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 8.29 [8.06] (s, 1H), 7.67–7.63 (m, 4H), 7.44–7.33 (m, 6H), 6.57 [7.18] (d, *J*=14.2 Hz, 1H), 5.01 [5.03] (dd, *J*=9.6, 14.2 Hz, 1H), 4.84 (dd, *J*=2.6, 9.6 Hz, 1H), 3.88 (m, 1H), 3.65 (t, *J*=6.9 Hz, 2H), 3.51 (dd, *J*=2.0, 6.9 Hz, 1H), 3.44 (m, 1H), 3.01 [3.03] (s, 3H), 2.58 (m, 1H), 2.48 (m, 1H, –OH), 2.13 [2.12] (s, 3H), 1.85–1.38 (m, 9H), 1.05 (d, *J*=6.6 Hz, 3H), 1.04 (s, 9H), 0.90 (d, *J*=6.6 Hz, 3H), 0.85 (d, *J*=6.6 Hz, 3H), 0.83 (s, 18H), 0.78 (d, *J*=6.9 Hz, 3H), 0.01 (s, 3H), 0.00 (s, 3H), −0.02 (s, 6H). The minor counterparts of doubled signals in the ratio of 2:1 due to the rotamers are in brackets; MS (FAB) *m/z* 920 $(M+Na)^+$.

3.1.86. Dimethylalanine ester 101. The experimental procedure was similar to that described for compound **29**. **101** (76% yield, *S*/*R*=3:1): a colorless oil; $[\alpha]_D^{29}=-13.4$ (*c* 0.118, $CHCl_3$); IR ($CHCl_3$) 1730, 1690, 1655, 1470, 1460, 1250, 1215, 1110, 1080 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 [8.03][a] (s, 1H), 7.66–7.63 (m, 4H), 7.44–7.35 (m, 6H), 6.48 [7.16][a] (d, *J*=14.2 Hz, 1H), 5.01–4.93 (m, 2H), 4.78 (dd, *J*=3.4, 9.8 Hz, 1H), 3.87 (m, 1H), 3.64 (t, *J*=6.8 Hz, 2H), 3.49 (m, 1H), 3.22 (m, 1H), 2.99 [3.00][b] (s, 3H), 2.55 (m, 1H), 2.37 [2.34][b] (s, 6H), 2.07 [2.06][a] (s, 3H), 1.85–1.25 (m, 13H), 1.04 (s, 9H), 1.02 [1.01][b] (d, *J*=6.8 Hz, 3H), 0.93 [0.92][b] (d, *J*=7.3 Hz, 3H), 0.91 [0.89][b] (d, *J*=7.3 Hz, 3H), 0.83 (s, 9H), 0.82 (s, 9H), 0.76 (d, *J*=6.8 Hz, 3H), 0.00 (s, 3H), −0.01 [0.00][a] (s, 3H), −0.02 (s, 3H), −0.03 [−0.02][a] (s, 3H). The minor counterparts of doubled signals in the ratios of 2:1 (superscript a), and 3:1 (superscript b) are in brackets; MS (FAB) *m/z* 1018 $(M+Na)^+$.

3.1.87. Analog 102. The experimental procedure was similar to that described for compound **32**. **102** (82% yield, *S*/*R*=3:1): a colorless oil; $[\alpha]_D^{32}=-27.3$ (*c* 0.038, $CHCl_3$); IR (film) 3400 (br), 3320, 1730, 1690, 1655, 1620, 1580, 1540, 1455, 1435, 1375, 1310, 1235, 1175, 1090, 1070, 1045 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 8.34 [8.08][a] (s, 1H), 6.82 [7.13][a] (d, *J*=14.2 Hz, 1H), 5.18–5.00 (m, 2H), 4.78 [4.79][b] (dd, *J*=2.4, 10.3 Hz, 1H), 4.36 (br s, 1H, –OH), 4.16 (dd, *J*=1.0, 9.3 Hz, 1H), 4.11 (br s, 1H, –OH), 4.08 (t, *J*=6.8 Hz, 2H), 3.29 (m, 1H), 3.17 (m, 1H), 2.94 [3.06][a] (s, 3H), 2.62 (m, 1H), 2.31 [2.50][a] [2.31][b] (s, 6H), 1.76–1.49 (m, 10H), 1.23 [1.24][b] (d, *J*=7.3 Hz, 3H), 0.98 [0.99][b] (d, *J*=7.3 Hz, 6H), 0.89 [0.90][b] (d, *J*=6.8 Hz, 6H). Signals of three protons (CH_3COO) were overlapped with the solvent signals. The minor counterparts of doubled signals in the ratios of 2:1 (superscript a), and 3:1 (superscript b) are in brackets; MS (FAB) *m/z* 553 $(M+Na)^+$; HRMS (FAB) calcd for $C_{27}H_{50}N_2NaO_8$ $[(M+Na)^+]$ 553.3465, found 553.3440.

3.1.88. Sulfone 103. A solution of sulfone **16** (108 mg, 0.126 mmol) in DME (8 mL) and 1 M HCl (2 mL) was stirred at room temperature for 4 h. The mixture was poured into ice-cooled saturated aqueous $NaHCO_3$ (6 mL), and the aqueous mixture was extracted with Et_2O (3×10 mL). The combined extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (6 g, hexane–acetone 2:1→1:1→1:2) to give a diastereomeric mixture of hemiacetals (75.3 mg).

A solution of the hemiacetals (75.3 mg) and $NaBH_4$ (9.7 mg, 0.26 mmol) in EtOH (2 mL) was stirred at room temperature for 45 min. Sodium borohydride (10.5 mg, 0.28 mmol) was added, and the reaction mixture was stirred for 45 min. Furthermore, $NaBH_4$ (6.5 mg, 0.17 mmol) was added, and the reaction mixture was stirred for 45 min. The mixture was diluted with saturated NH_4Cl (5 mL) and extracted with EtOAc (3×10 mL). The combined extracts were washed with brine (2 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (6 g, CH_2Cl_2–acetone 4:1→acetone→MeOH) to give a tetraol (80.5 mg).

A solution of the tetraol (76.5 mg) in 1,4-dioxane (4.5 mL) and 2 M HCl (1.5 mL) was stirred at 50°C for 2 h. The mixture was poured into ice-cooled saturated aqueous $NaHCO_3$ (6 mL), and the aqueous mixture was extracted with EtOAc (3×10 mL). The combined extracts were washed with brine (3 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (6 g, $CHCl_3$–MeOH 20:1→15:1→10:1) to give a pentaol (33.0 mg).

A solution of the pentaol (31.5 mg), DMAP (2.8 mg, 0.023 mmol), Et_3N (0.012 mL, 0.086 mmol), and *t*-$BuMe_2$-SiCl (11.1 mg, 0.074 mmol) in CH_2Cl_2 (0.5 mL) was stirred at room temperature for 1 h. DMAP (6.8 mg, 0.056 mmol) and *t*-$BuMe_2SiCl$ (6.2 mg, 0.041 mmol), and Et_3N (0.005 mL, 0.036 mmol) were added to the reaction mixture, and

the mixture was stirred at room temperature for 2 h. Furthermore, *t*-BuMe$_2$SiCl (6.4 mg, 0.042 mmol) and Et$_3$N (0.005 mL, 0.036 mmol) were added, and the mixture was stirred at room temperature for 30 min, diluted with ice water (1 g), and extracted with EtOAc (3×5 mL). The combined extracts were washed successively with 1 M HCl (2 mL), saturated aqueous NaHCO$_3$ (2 mL), and brine (2 mL), and then dried (Na$_2$SO$_4$) and concentrated. The residue was purified by column chromatography on silica gel (5 g, CH$_2$Cl$_2$–acetone 4:1→1:1) to give **103** (34.5 mg, 51% from **16**) as a colorless oil: $[\alpha]_D^{30}=-12.7$ (*c* 1.11, CHCl$_3$); IR (CHCl$_3$) 3495–3100, 1460, 1380, 1255, 1150, 1085, 1030, 975, 840 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92 (dd, *J*=1.5, 6.8 Hz, 2H), 7.66 (tt, *J*=1.5, 7.3 Hz, 1H), 7.57 (dd, *J*=6.8, 7.3 Hz, 2H), 4.47 (d, *J*=3.9 Hz, 1H, –OH), 3.99 (br d, *J*=1.5 Hz, 1H, –OH), 3.94–3.86 (m, 2H), 3.78 (ddd, *J*=3.4, 7.3, 10.7 Hz, 1H), 3.65 (ddd, *J*=3.4, 7.3, 10.7 Hz, 1H), 3.64 (d, *J*=3.9 Hz, 1H, –OH), 3.40 (ddd, *J*=4.9, 10.7, 14.2 Hz, 1H), 3.44–3.33 (m, 2H), 3.14 (ddd, *J*=4.9, 10.7, 14.2 Hz, 1H), 3.08 (d, *J*=4.4 Hz, 1H, –OH), 2.01–1.87 (m, 2H), 1.83–1.57 (m, 7H), 1.54–1.41 (m, 2H), 1.16 (m, 1H), 0.97 (d, *J*=6.8 Hz, 3H), 0.93 (d, *J*=7.3 Hz, 3H), 0.92–0.90 (m, 3H), 0.90 (s, 9H), 0.88 (d, *J*=6.8 Hz, 3H), 0.08 (s, 6H); MS (FAB) *m*/*z* 611 (M+Na)$^+$.

3.1.89. TES ether 104. A solution of sulfone **103** (34.5 mg, 0.059 mmol), imidazole (65 mg, 0.96 mmol), and Et$_3$SiCl (0.080 mL, 0.48 mmol) in DMF (0.5 mL) was stirred at room temperature for 30 min and at 40°C for 75 min. The mixture was diluted with ice water (2 g) and extracted with Et$_2$O (3×5 mL). The combined extracts were washed with brine (2 mL), dried (Na$_2$SO$_4$), and concentrated. The residue was purified by column chromatography on silica gel (5 g, hexane–Et$_2$O 15:1→10:1) to give **104** (54.2 mg, 88%) as a colorless oil: $[\alpha]_D^{31}=-0.74$ (*c* 0.41, CHCl$_3$); IR (CHCl$_3$) 1460, 1415, 1380, 1310, 1240, 1145, 1085, 1010, 970, 835 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91–7.89 (m, 2H), 7.66 (m, 1H), 7.59–7.55 (m, 2H), 3.86–3.78 (m, 2H), 3.68 (ddd, *J*=4.4, 7.3, 10.3 Hz, 1H), 3.60–3.54 (m, 2H), 3.42 (dd, *J*=2.4, 6.8 Hz, 1H), 3.12 (ddd, *J*=5.9, 11.7, 13.7 Hz, 1H), 3.02 (ddd, *J*=5.9, 10.7, 13.7 Hz, 1H), 1.94–1.24 (m, 12H), 0.95 (t, *J*=7.8 Hz, 18H), 0.93 (t, *J*=7.8 Hz, 9H), 0.93–0.89 (m, 3H), 0.90 (t, *J*=7.8 Hz, 9H), 0.89 (s, 9H), 0.84 (d, *J*=6.8 Hz, 3H), 0.77 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.8 Hz, 3H), 0.68–0.49 (m, 24H), 0.04 (s, 6H); MS (FAB) *m*/*z* 1067 (M+Na)$^+$.

3.1.90. Olefin 105 and the *cis*-isomer. The experimental procedure was similar to that described for compound **17**. **105** (70% yield): a colorless oil; $[\alpha]_D^{28}=+21.1$ (*c* 1.39, CHCl$_3$); IR (CHCl$_3$) 1720, 1460, 1380, 1285, 1255, 1165, 1090, 1050, 1005, 970, 835 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.52 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.34 (dd, *J*=7.3, 7.3 Hz, 1H), 5.23 (dd, *J*=8.3, 15.1 Hz, 1H), 4.64 (d, *J*=11.7 Hz, 1H), 4.58 (d, *J*=11.7 Hz, 1H), 4.20–4.09 (m, 2H), 3.97 (m, 1H), 3.87 (m, 1H), 3.70–3.51 (m, 6H), 3.49 (dd, *J*=3.9, 3.9 Hz, 1H), 3.37 (dd, *J*=6.8, 6.8 Hz, 1H), 3.22 (s, 3H), 3.15 (s, 3H), 2.30 (m, 2H), 2.16 (s, 3H), 2.15 (m, 1H), 1.96 (m, 1H), 1.87–1.20 (m, 21H), 1.49 (s, 3H), 1.20 (s, 9H), 0.99–0.87 (m, 12H), 0.97 (t, *J*=7.8 Hz, 9H), 0.96 (t, *J*=7.8 Hz, 18H), 0.94 (t, *J*=7.8 Hz, 9H), 0.89 (s, 18H), 0.88 (d, *J*=6.8 Hz, 3H), 0.79 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.8 Hz, 3H), 0.65–0.58 (m, 24H), 0.05 (s, 3H), 0.04 (s, 6H); MS (FAB) *m*/*z* 1569 (M+Na)$^+$. *cis*-Isomer (7% yield): a colorless oil; $[\alpha]_D^{29}=+23$ (*c* 0.24, CHCl$_3$); IR (CHCl$_3$) 1720, 1460, 1380, 1285, 1255, 1160, 1090, 1050, 1035, 970, 835 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.55 (ddd, *J*=6.8, 6.8, 10.7 Hz, 1H), 5.34 (dd, *J*=6.8, 6.8 Hz, 1H), 5.24 (dd, *J*=9.8, 10.7 Hz, 1H), 4.64 (d, *J*=11.2 Hz, 1H), 4.58 (d, *J*=11.2 Hz, 1H), 4.21–4.08 (m, 2H), 4.04–3.95 (m, 2H), 3.85 (m, 1H), 3.71–3.52 (m, 5H), 3.49 (dd, *J*=3.9, 3.9 Hz, 1H), 3.37 (dd, *J*=6.8, 6.8 Hz, 1H), 3.26 (s, 3H), 3.15 (s, 3H), 2.44–2.26 (m, 3H), 2.17 (m, 1H), 2.16 (s, 3H), 1.96 (m, 1H), 1.86–1.16 (m, 20H), 1.50 (s, 3H), 1.20 (s, 9H), 0.99–0.87 (m, 15H), 0.97 (t, *J*=7.8 Hz, 9H), 0.95 (t, *J*=7.8 Hz, 18H), 0.94 (t, *J*=7.8 Hz, 9H), 0.89 (s, 18H), 0.80 (d, *J*=6.8 Hz, 3H), 0.77 (d, *J*=7.3 Hz, 3H), 0.65–0.55 (m, 24H), 0.05 (s, 3H), 0.04 (s, 9H); MS (FAB) *m*/*z* 1569 (M+Na)$^+$.

3.1.91. Alcohol 106. The experimental procedure was similar to that described for compound **18**. **106** (100% yield): a colorless oil; $[\alpha]_D^{29}=+29.6$ (*c* 1.04, CHCl$_3$); IR (CHCl$_3$) 3480 (br), 1595, 1515, 1465, 1380, 1260, 1095, 1030, 970, 835 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.53 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.34 (dd, *J*=7.3, 7.3 Hz, 1H), 5.23 (dd, *J*=8.3, 15.1 Hz, 1H), 4.70 (d, *J*=11.7 Hz, 1H), 4.59 (d, *J*=11.7 Hz, 1H), 3.97 (m, 1H), 3.87 (m, 1H), 3.82–3.65 (m, 4H), 3.60–3.51 (m, 4H), 3.49 (dd, *J*=3.4, 4.9 Hz, 1H), 3.38 (dd, *J*=6.8, 6.8 Hz, 1H), 3.22 (s, 3H), 3.16 (s, 3H), 2.50 (br s, 1H, –OH), 2.31 (m, 2H), 2.21 (s, 3H), 2.14 (m, 1H), 1.98 (m, 1H), 1.88–1.21 (m, 21H), 1.50 (s, 3H), 0.99–0.87 (m, 15H), 0.97 (t, *J*=7.8 Hz, 9H), 0.96 (t, *J*=7.8 Hz, 18H), 0.94 (t, *J*=7.8 Hz, 9H), 0.89 (s, 9H), 0.89 (s, 9H), 0.80 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.8 Hz, 3H), 0.65–0.58 (m, 24H), 0.05 (s, 3H), 0.04 (s, 9H); MS (FAB) *m*/*z* 1485 (M+Na)$^+$.

3.1.92. Aldehyde 107. The experimental procedure was similar to that described for compound **19**. **107** (89% yield): a colorless oil; $[\alpha]_D^{26}=+13.3$ (*c* 1.03, CHCl$_3$); IR (CHCl$_3$) 2730, 1720, 1460, 1380, 1360, 1285, 1255, 1165, 1095, 1045, 835 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.82 (dd, *J*=2.0, 2.4 Hz, 1H), 5.53 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.34 (dd, *J*=6.8, 6.8 Hz, 1H), 5.23 (dd, *J*=8.3, 15.1 Hz, 1H), 4.67 (d, *J*=11.7 Hz, 1H), 4.60 (d, *J*=11.7 Hz, 1H), 4.06 (ddd, *J*=3.9, 5.9, 7.3 Hz, 1H), 3.97 (ddd, *J*=2.4, 4.9, 7.3 Hz, 1H), 3.87 (m, 1H), 3.68 (ddd, *J*=4.4, 7.3, 9.8 Hz, 1H), 3.60–3.50 (m, 5H), 3.38 (dd, *J*=6.8, 6.8 Hz, 1H), 3.22 (s, 3H), 3.16 (s, 3H), 2.59 (ddd, *J*=2.4, 7.3, 16.6 Hz, 1H), 2.53 (ddd, *J*=2.0, 3.9, 16.6 Hz, 1H), 2.31 (m, 2H), 2.14 (s, 3H), 2.14 (m, 1H), 2.00 (m, 1H), 1.86–1.21 (m, 20H), 1.50 (s, 3H), 0.99–0.76 (m, 12H), 0.97 (t, *J*=7.8 Hz, 9H), 0.96 (t, *J*=7.8 Hz, 19H), 0.94 (t, *J*=7.8 Hz, 9H), 0.89 (s, 9H), 0.89 (s, 9H), 0.88 (d, *J*=7.3 Hz, 3H), 0.80 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.8 Hz, 3H), 0.65–0.56 (m, 24H), 0.07 (br s, 3H), 0.05 (s, 3H), 0.04 (s, 6H); MS (FAB) *m*/*z* 1483 (M+Na)$^+$.

3.1.93. α,β,γ,δ-Unsaturated ester 108. The experimental procedure was similar to that described for compound **20**. **108** (89% yield): a colorless oil; $[\alpha]_D^{27}=+1.17$ (*c* 0.915, CHCl$_3$); IR (CHCl$_3$) 1700, 1640, 1620, 1460, 1415, 1370, 1300, 1255, 1085, 1045, 970, 835 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.27 (dd, *J*=10.3, 15.1 Hz, 1H), 6.28–6.13 (m, 2H), 5.80 (d, *J*=15.1 Hz, 1H), 5.52 (ddd, *J*=7.3,

7.3, 15.1 Hz, 1H), 5.34 (dd, *J*=7.3, 7.3 Hz, 1H), 5.23 (dd, *J*=8.3, 15.1 Hz, 1H), 4.67 (d, *J*=11.7 Hz, 1H), 4.58 (d, *J*=11.7 Hz, 1H), 4.20 (q, *J*=7.3 Hz, 2H), 3.97 (m, 1H), 3.87 (m, 1H), 3.68 (ddd, *J*=4.4, 7.3, 10.3 Hz, 1H), 3.61 (dd, *J*=3.9, 3.9 Hz, 1H), 3.58–3.51 (m, 5H), 3.38 (dd, *J*=6.8, 6.8 Hz, 1H), 3.22 (s, 3H), 3.16 (s, 3H), 2.45 (ddd, *J*=3.4, 5.4, 15.6 Hz, 1H), 2.36–2.27 (m, 3H), 2.15 (m, 1H), 2.14 (s, 3H), 1.87–1.26 (m, 18H), 1.50 (s, 3H), 1.29 (t, *J*=7.3 Hz, 3H), 0.99–0.76 (m, 12H), 0.97 (t, *J*=7.8 Hz, 9H), 0.96 (t, *J*=7.8 Hz, 18H), 0.96 (m, 1H), 0.94 (t, *J*=7.8 Hz, 9H), 0.89 (s, 9H), 0.89 (s, 9H), 0.88 (d, *J*=7.3 Hz, 3H), 0.80 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.8 Hz, 3H), 0.65–0.56 (m, 24H), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 6H); MS (FAB) *m/z* 1579 $(M+Na)^+$.

3.1.94. Alcohol 109. The experimental procedure was similar to that described for compound **30**. **109** (80% yield): a colorless oil; $[\alpha]_D^{28}=+7.5$ (*c* 0.49, $CHCl_3$); IR ($CHCl_3$) 3450 (br), 1700, 1640, 1615, 1460, 1415, 1370, 1255, 1090, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, *J*=9.8, 15.1 Hz, 1H), 6.30–6.18 (m, 2H), 5.81 (d, *J*=15.1 Hz, 1H), 5.52 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.34 (dd, *J*=6.8, 6.8 Hz, 1H), 5.22 (dd, *J*=8.3, 15.1 Hz, 1H), 4.20 (q, *J*=7.3 Hz, 2H), 3.97 (ddd, *J*=2.4, 5.4, 7.8 Hz, 1H), 3.87 (m, 1H), 3.75 (dd, *J*=2.0, 4.9 Hz, 1H), 3.71–3.63 (m, 2H), 3.60–3.51 (m, 4H), 3.38 (dd, *J*=6.8, 6.8 Hz, 1H), 3.22 (s, 3H), 3.16 (s, 3H), 3.01 (m, 1H, –OH), 2.48 (ddd, *J*=3.9, 5.4, 15.6 Hz, 1H), 2.30 (m, 2H), 2.26–2.10 (m, 2H), 2.14 (s, 3H), 1.87–1.26 (m, 19H), 1.50 (s, 3H), 1.29 (t, *J*=7.3 Hz, 3H), 0.97 (t, *J*=7.8 Hz, 9H), 0.96 (t, *J*=7.8 Hz, 18H), 0.96 (m, 1H), 0.94 (t, *J*=7.8 Hz, 9H), 0.90–0.87 (m, 9H) 0.90 (s, 9H), 0.89 (s, 9H), 0.88 (d, *J*=6.8 Hz, 3H), 0.83 (d, *J*=6.8 Hz, 3H), 0.79 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.8 Hz, 3H), 0.62 (q, *J*=7.8 Hz, 6H), 0.61 (q, *J*=7.8 Hz, 18H), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 6H); MS (FAB) *m/z* 1519 $(M+Na)^+$.

3.1.95. Trimethylserine ester 110. The experimental procedure was similar to that described for compound **31**. **110** (86% yield, *S*/*R*=1.3:1): a colorless oil; $[\alpha]_D^{31}=-8.6$ (*c* 0.45, MeOH); IR ($CHCl_3$) 1710, 1645, 1620, 1460, 1415, 1370, 1255, 1090, 1040, 970, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, *J*=10.7, 15.1 Hz, 1H), 6.31 (m, 1H), 6.23 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.95 (d, *J*=15.1 Hz, 1H), 5.59 (ddd, *J*=7.3, 7.3, 15.1 Hz, 1H), 5.39 (dd, *J*=7.3, 7.3 Hz, 1H), 5.29 (dd, *J*=7.8, 15.1 Hz, 1H), 4.92 (m, 1H),4.14 (q, *J*=7.3 Hz, 2H), 4.07 (m, 1H), 4.00 (m, 1H), 3.73 (ddd, *J*=4.4, 7.3, 10.3 Hz, 1H), 3.68–3.55 (m, 7H), 3.43–3.36 (m, 2H), 3.30 (s, 3H), 3.21 (s, 3H), 3.12 [3.12] (s, 3H), 2.64 (m, 1H), 2.49–2.32 (m, 5H), 2.37 [2.33] (s, 6H), 2.16 (m, 1H), 2.08–0.98 (m, 18H), 1.51 (s, 3H), 1.23 (t, *J*=7.3 Hz, 3H), 1.00 (t, *J*=7.8 Hz, 27H), 1.00 (t, *J*=7.8 Hz, 9H), 0.94–0.89 (m, 15H), 0.92 (s, 9H), 0.90 (s, 9H), 0.87 (d, *J*=7.3 Hz, 3H), 0.83 (d, *J*=6.8 Hz, 3H), 0.72–0.62 (m, 24H), 0.16 (s, 3H), 0.11 [0.10] (s, 3H), 0.07 [0.06] (s, 3H), 0.06 (s, 6H). The counterparts of doubled signals in the ratios of 1.3:1 are in brackets; MS (FAB) *m/z* 1648 $(M+Na)^+$.

3.1.96. Acyclic analog 111. The experimental procedure was similar to that described for compound **32**. **111** (75% yield, *S*/*R*=1.3:1): a colorless oil; $[\alpha]_D^{31}=-16$ (*c* 0.428, MeOH); UV (MeCN) λ_{max} 258 nm (ε 29,000); IR ($CHCl_3$) 3615, 3490 (br), 1705, 1645, 1640, 1620, 1460, 1370, 1305 1250, 1180, 1090, 975 cm^{-1}; ^1H NMR (600 MHz, acetone-d_6) δ 7.22 (dd, *J*=10.6, 15.0 Hz, 1H), 6.34 (m, 1H), 6.22 (m, 1H), 5.84 (d, *J*=15.0 Hz, 1H), 5.68 (ddd, *J*=7.3, 7.3, 15.0 Hz, 1H), 5.36 (dd, *J*=7.3, 7.3 Hz, 1H), 5.28 (dd, *J*=8.4, 15.0 Hz, 1H), 5.04 (ddd, *J*=3.7, 3.7, 7.7 Hz, 1H), 4.42 (br s, 1H), 4.13 (q, *J*=7.3 Hz, 2H), 4.11 (br s, 1H), 4.05 (dd, *J*=6.6, 6.6 Hz, 1H), 3.97–3.91 (m, 2H), 3.85 (br s, 1H), 3.78 (br s, 1H), 3.69–3.63 (m, 2H), 3.60–3.54 (m, 3H), 3.41–3.26 (m, 5H), 3.28 [3.29] (s, 3H), 3.19 (br s, 1H), 3.17 (s, 3H), 3.10 (s, 3H), 2.67 (m, 1H), 2.47 (ddd, *J*=7.7, 7.7, 15.4 Hz, 1H), 2.31 [2.33] (s, 6H), 2.28 (m, 1H), 2.20 (m, 1H), 2.09 (m, 1H), 1.96–1.74 (m, 8H), 1.66 (m, 2H), 1.57–1.40 (m, 8H), 1.49 (s, 3H), 1.23 (t, *J*=7.3 Hz, 3H), 1.11–0.95 (m, 2H), 0.96 (d, *J*=7.0 Hz, 3H), 0.92–0.88 (m, 3H), 0.91 (d, *J*=6.2 Hz, 3H), 0.89 (d, *J*=6.6 Hz, 3H), 0.76 [0.80] (d, *J*=6.6 Hz, 3H). The counterparts of doubled signals in the ratios of 1.3:1 are in brackets; MS (FAB) *m/z* 964 $(M+Na)^+$; HRMS (FAB) calcd for $C_{52}H_{95}NNaO_{13}$ $[(M+Na)^+]$ 964.6701, found 964.6725.

3.2. Cytotoxic activity

The cytotoxicity was observed by Dr Hisao Ekimoto and Ms Mutsuko Kimura (Nippon Kayaku Co., Ltd) using the reported procedure.[25]

3.3. Measurement of flow birefringence

Actin was extracted in cold water from the acetone-dried powder of rabbit skeletal muscle, purified,[26] and polymerized in 100 mM KCl, 5 mM Tris-HCl (pH 8.0), 0.2 mM ATP, and 1 mM DTT before use. The test compounds were dissolved in DMSO and added to the F-actin solution (40 μM). The incubated actin solutions (room temperature, 1 min) were analyzed in a micro FBR-Mark II apparatus (Wakenyaku Co., Kyoto, Japan) with rotation at 500 rpm. The IC_{50} values were calculated as the concentrations of the test compounds required to reduce the flow birefringence of the F-actin solution (40 μM) to 50% of its control amplitude. The final concentration of DMSO added to the reaction mixtures with the test compounds was 1% (v/v) except for compounds **64**, **67** and **89** (5–10%, v/v). The IC_{50} values are mean values of at least three experiments.

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